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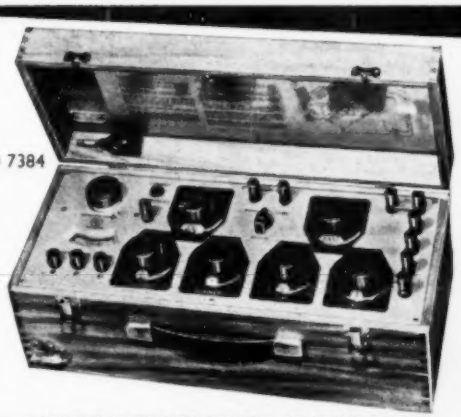

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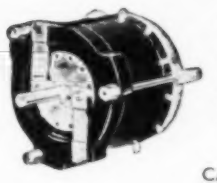

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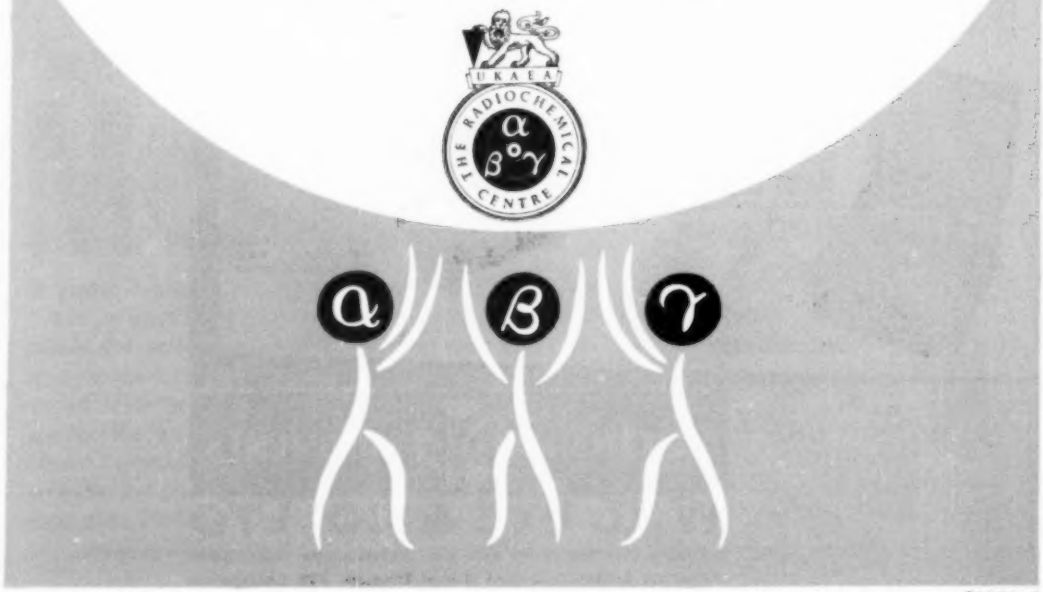

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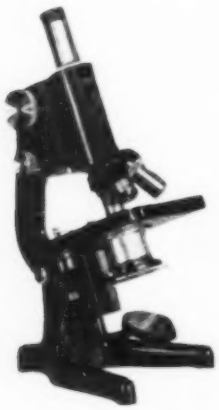

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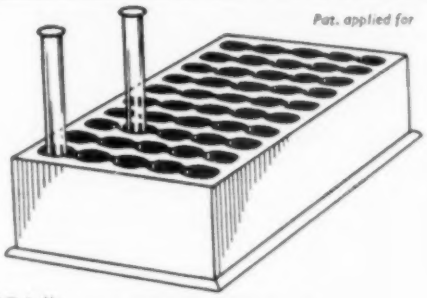

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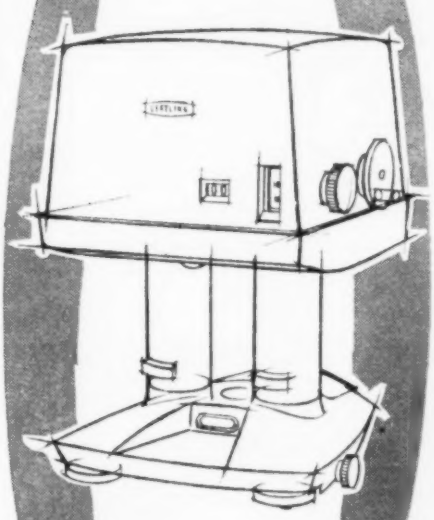

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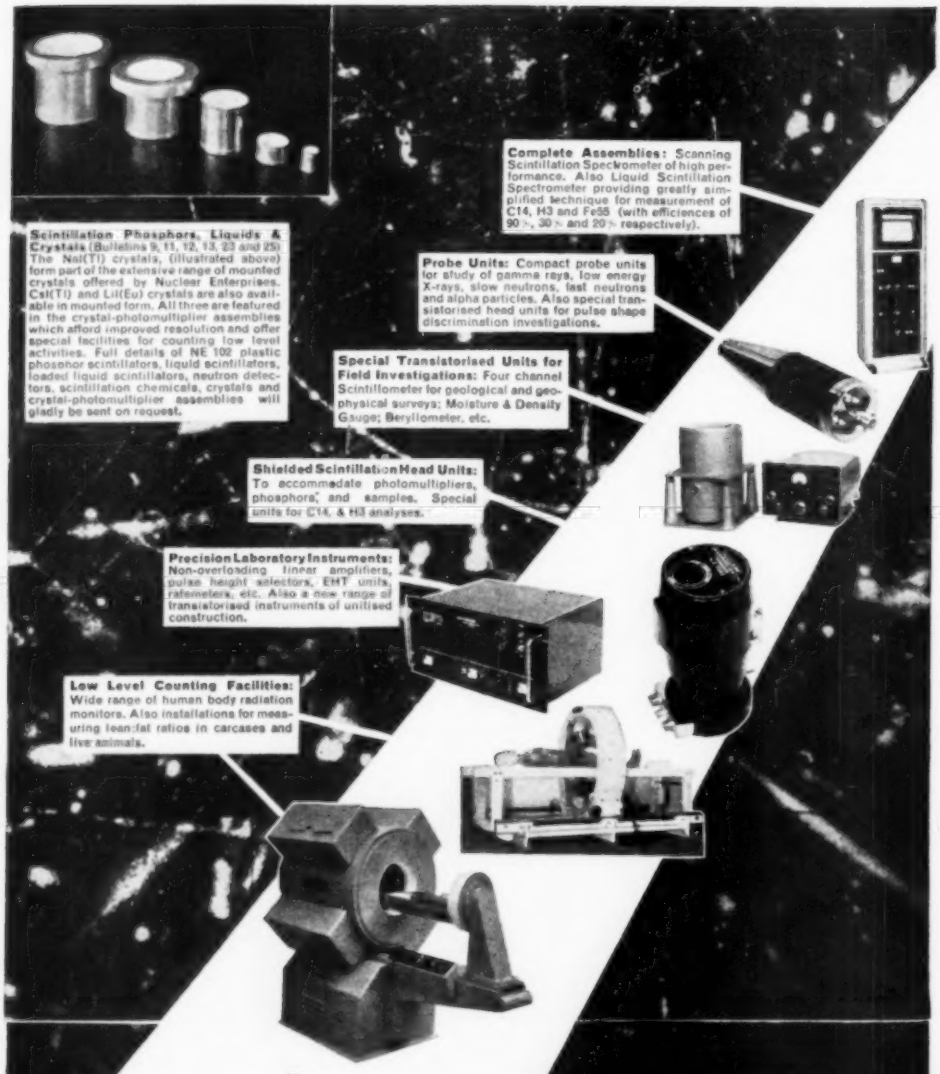

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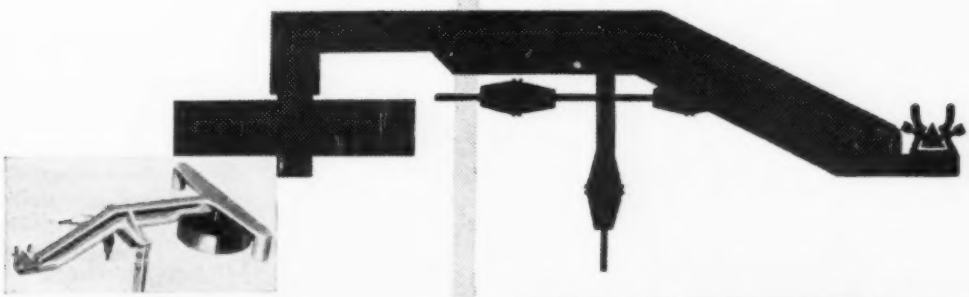

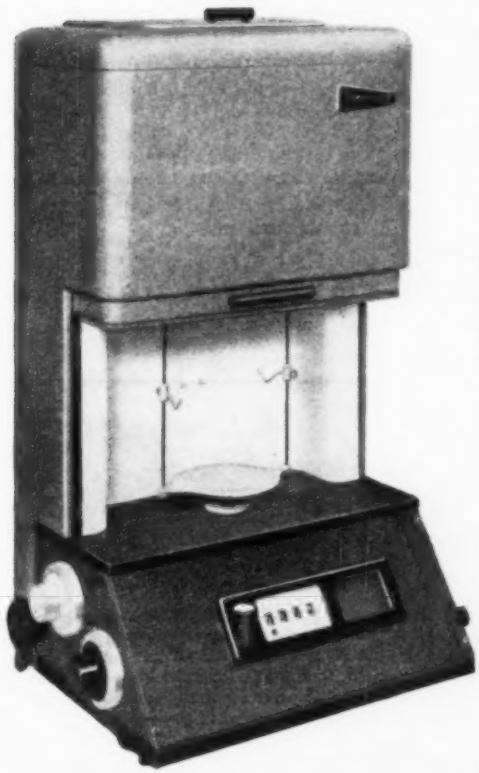

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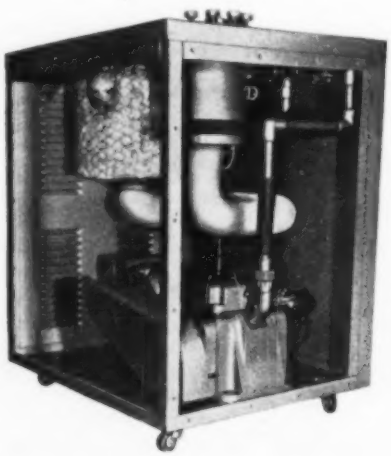

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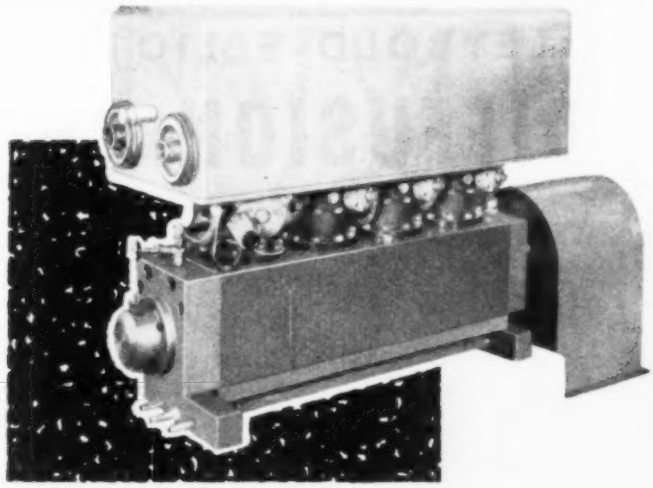

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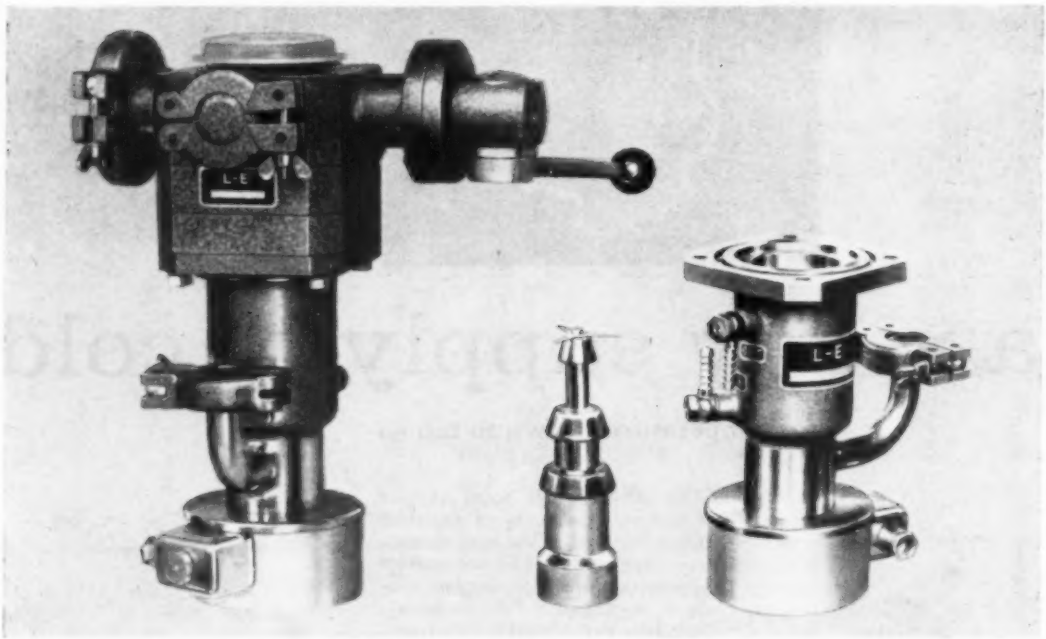

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We are glad to be able to announce that the third printing of Mr. Holland's book, first published five years ago, is now ready, and we regret that the new impression has taken somewhat longer to produce than was anticipated. When the book originally appeared it received wide and justified commendation from reviewers in a great number of scientific journals in the United Kingdom and throughout the world. There is no doubt of the continuing demand for what is now generally recognized as a standard work on the subject. *Illustrated. 70s.*

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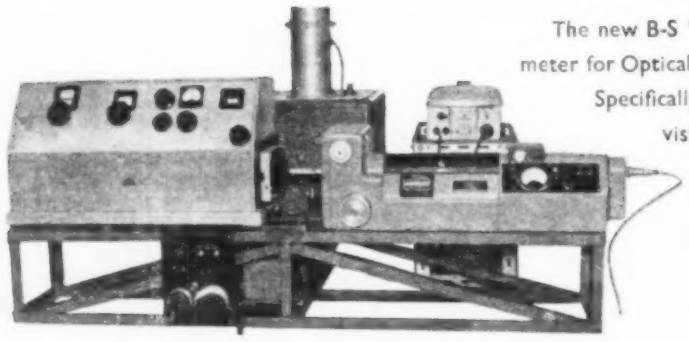

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AN EDUCATION FOR LIFE

ONE cannot help but feel a pang of sympathy for the youth of Britain to-day, gazing wide-eyed at the promised good (or goods) of our technological era. For it seems that the promised good may conceal and nurture a stifling evil.

In a report arising from the annual conference of the British Association for Commercial and Industrial Education*, critical surveys of recent policy recommendations in the field of education are presented. A final article summarizes these very aptly. It also proffers the happy conjecture that in A.D. 3000 posterity, on finding the Crowther, Albemarle, Carr, Jackson, McMeeking, Arnold and Anderson Reports in a casket, will experience a positive reaction to the energy and vision that was contributed to reassessing education for British youth.

The need for all this drastic reform springs from "a pressure quite outside the scope of public control, for its comes from outside . . . relates to the position of Great Britain among her trade competitors in other countries and the influence upon this of the system of higher education in this country". The old order of education whereby men were equipped with a "proper background" must yield to the new scheme of "indoctrinating them with certain forms of knowledge". They must now train to be of direct use to improve industrial processes and products. The knell of industry sounds ever shriller. Specialize, 'technologize' or perish. Hence, happily or otherwise, the country must eddy along in this sweeping technological turbulence.

In the teeth of the gale of change, perhaps we should try to preserve some degree of self-control, however, and not throw out existing good as so much ballast. To persuade the keenest minds of our generation into a technological career as the glowing imperative, could result in irrecoverable loss, particularly when it conflicts with natural tendencies in other directions. It is not fair. Some personalities, some minds, are suited to such a career, others not. Almost platitudinous, it may be said ; but then a platitude has been defined as a self-evident fact on which nobody acts.

To get the cream of British minds recruited to serve technology, we eulogize the virtues of applied science—'it performs everything by the surest rules and demonstrations'—in the Baconian sense. But we tend to gloss over the pedestrian qualities which are inescapably there. We show that the job of an applied scientist is to evaluate coefficients of the differential equations which physicists and mathematicians have formulated long before. This job is done using experiment, curve-fitting, statistical manipulation and computers when the mathematics is not amenable to implicit, analytical solutions. Useful and skilled activity, to be sure, but we may tend to glorify it as a creative process of the highest order, forgetting that what one technologist learns to manipulate, another can. Our unbridled enthusiasm may lead us to believe that training a man to be a directly useful component in industry is the *raison d'être* of education. Perhaps we should be a trifle more restrained and tell those brighter youths, who wish to do creative work, that a career in technology is very often a consuming, grim grind and a quest for half-truths.

The educational system of a country is an expression of its national ideal. Despite the obloquy levelled against the British system from inside, one cannot deny that it has produced men eminently civilized and competent. Turn to the international arena, where the unfortunate East–West technocracies clash, and note the undisguised, fierce barbarism on one hand and the poorly disguised sentimentality and emasculation on the other. Then look at Europe, with Britain, and recognize quality. In the past, as now still, British education served to produce men who were literate, able to reflect, to judge and to converse. They understood the broad sweep of things. In a recent article*, Prof. M. W. Thring adduces that to-day "we have the much more concrete problem of making scientific laws seem exciting and interesting to a large proportion of our youth". What a pity that we must make these laws only seem so. Do we fall into inadvertent deception to serve the great-god, 'Technology' ? Must the "combustible material" in the minds of our youth (Prof. Thring's imagery) be made a burnt-offering to the avaricious deity ?

The British have always shown a proclivity to retain what they have proved good over centuries. Now we are beginning to distrust our judgment. Trans-Atlantic fever for uprooting itself fascinates : "In America industrial management will very often scrap plant just because something newer has come along. . . . We keep old plant because we are fond of it. . . ." We gaze bewitched at the Kremlin and Peking ; the Labour University at Kiangsi has 50,000 students and there are 1,065 such institutions in China. What a paradisial plethora of technologists there must be. Instead of being naïvely deceived as to what constitutes quality, we should pause and consider where the fount of fundamental scientific ideas springs from, and then note the educational environment which has given rise to these meditative, inspired minds.

We have indeed a grave responsibility to British youth. Let not the national ideal be to turn out mass-produced stereotypes who cannot converse or use language properly except as the jargon of their particular narrow occupation, who seek only to speak of facts, dull though these may be, who

* Policy in Perspective : Report of the BACIE Annual Conference held at Cambridge, 22–24 September, 1960. Pp. 126. (London : British Association for Commercial and Industrial Education, 1960.) 10*s*.

* *The Advancement of Science*, Vol. 17, No. 69 ; January 1961. Pp. 456–460. (London : British Association for the Advancement of Science, 1961.) 7*s*. 6*d*.

cannot stand up to dialectical encounter, who show distinct discomfort when ideas, feelings and imagination are introduced. Let us respect the individual. Instead of forcing or trapping the talented into a technological constraint, let us rather guide them wisely toward, and allow them to flourish in, the environment to which they naturally would incline.

Amid the frenzied pressures of this decade, it seems appropriate to refer to the Earl Grey Memorial Lecture (*Today and Yesterday*) delivered by G. M. Young. He felt that the duty of a State is to build up a nation which, in the Aristotelian sense of the educated, the civilized mind, knows what questions to ask and what answers to be satisfied with. Before the passage from adolescence to manhood is complete, there should be implanted in the child an appreciation of domestic coherence, sense of stock, significance of the hearth and of the society which goes on and on for ever and is by nature the home. He should be guided in his education from the dogmatic stage, where there is passive acceptance, to the dialectical, where the infinite variety of interpretations of life is grasped. Here he, who is trained in a purely technical sense, often fails abysmally. Imbued with the rules and procedures of his precious doxology, anything outside his little province is scarcely credible, if at all comprehensible.

Mr. Young believes that people cannot be educated at a much greater rate than their families are being civilized. No doubt, however, if proper education becomes more and more available, greater numbers will emerge from homes where true intellectual sympathy reigns. With the canons of science and the art of reasoning so generally understood, the relationship between the learned and the ignorant would be one of confidence. So, even in the new order, Britain will preserve that sense or instinct of continuity: each generation being duly trained to step into the succession when the time comes. In effect, Britain would thus rear a democracy which was also an aristocracy. If no longer a great power, let us strive to be a good one.

So, beset by the dominant influences of the world to-day—fierce, passionate despotism on one side and sick, surrealistic anarchy on the other—Britain must eschew imitation. Instead, may the good bequeathed by the experience of ancestry be recognized and retained. May it continue, with Wordsworthian sentiment, "To make the gift of life more valuable and the men more worthy of the gift".

INTRODUCTION TO PLANT ANATOMY

Anatomy of Seed Plants

By Prof. Katherine Esau. Pp. xvi + 376. (New York: John Wiley and Sons, Inc.: London: Chapman and Hall, Ltd., 1960.) 56s. net.

IT is essential for all students of botany to make themselves well informed about the structure of plants. This applies to those who will ultimately become specialists as well as to those whose knowledge of botany remains more general. In spite of the importance of plant anatomy it is remarkable how seldom we find that a student's knowledge of this branch of botany reaches the same standard as that which he attains in others. This situation probably arises, at least in part, because there are so few botanists who are actively engaged on research into the classical aspects of plant histology, and teachers of the subject tend to be purveyors of second-hand information and lack the inspiration that can come only to those fighting in the front line to acquire new knowledge. Prof. Esau has, for many years, been actively engaged on plant anatomical research. She can therefore speak as one having authority based on first-hand experience, and, in the book under review, she does so in clear and simple language. She illustrates what she has to say with line drawings, photomicrographs and a few electron micrographs. These illustrations, of which only a few have been supplied by other authors, are well chosen and of quite outstanding quality. These facts will cause no surprise to the many students and research workers who are already familiar with Prof. Esau's larger text-book entitled *Plant Anatomy* (John Wiley and Sons Inc., 1953), which has come to be accepted as one of the best books of its kind in the English language. The high price of the larger book has, however, undoubtedly prevented it from being as widely used among impecunious students as it deserves to be, and the shortened version which Prof. Esau has now produced, although the price is still fairly high, can be sure of a ready welcome. Indeed, it is to be hoped that the carefully selected anatomical information which it contains will be mastered by all students of botany and that it will serve as the terra firma of fundamental knowledge on which their subsequent studies may be securely grounded.

The book is divided into 22 chapters. The subject is treated mainly from the developmental point of view and deals not only with the cells and tissues of adult organs, including those of flowers, fruits and seeds, but also treats the plant at all stages from the embryo to maturity. There are indications of how the structure of the plant is related to ecological conditions, to taxonomy and to physiology. There is little to be found to criticize in a book of such undoubted excellence and that is so well produced and printed, but the reviewer feels that the relationship of structure to physiological function could be usefully expanded. For example, where Prof. Esau is discussing phloem, on the structure of which she is indeed a leading authority, one is intrigued to read that the nature of the protoplasts of sieve-tube elements and of the connecting strands in sieve areas must be understood before we can reach a satisfactory explanation of how food is translocated. It is also interesting to read that "the known characters of the protoplast do not wholly support any of the hypotheses advanced so far with regard to the (translocation) mechanism". Having had his appetite thus whetted, the reader may well feel that he would like to know more about Prof. Esau's views on this all-important topic; but perhaps the explanation is that she has thought it wise not to commit herself too far in an elementary text-book.

Selected bibliographies are given at the ends of the chapters, and the book contains an excellent and all-important glossary of anatomical terms. Such glossaries are very much needed, especially in these days, when there is often a lack of precision in the meaning of terms, when the language employed by

wood anatomists is not always familiar to other anatomists, when pharmacognoscists sometimes tend to use terms in senses that do not always agree with those used in botany departments, and when electron microscopists and classical anatomists do not mean quite the same thing when they use a term as familiar as 'primary wall'. Most of the terms that Prof. Esau has adopted should be readily accepted by all, but botanists in Great Britain may be surprised to find the white- and yellow-coloured tissue in the rind of an orange referred to as the 'albedo' and 'flavedo' respectively.

Prof. Esau lays special emphasis on the unity and interdependence of the parts of a plant as revealed by developmental studies. This unity is further stressed in the introduction to this book where we read that: "The separation of the plant into organs can be made only approximately. It is impossible, for example, to draw a clear demarcation between the shoot and root and between stem and leaf, and the flower in many ways resembles the vegetative shoot. The internal structures, similarly, are not sharply delimited, and the categories of cells and tissues show much intergrading". How true this all is, and how helpful it would be if it were more generally recognized among botanists that Nature abhors distinct lines of demarcation. The classification of cells and tissues, like that of the plants themselves, is by no means easy.

In this book the author successfully vitalizes the whole subject, and the reader can scarcely fail to realize at the outset that he is being asked to consider cells and tissues in living organisms and not in dead corpses. It is to be hoped that this vital approach will stimulate a widespread desire among students to know more about this important aspect of plant science which is often so needlessly thought of as being dull.

C. R. METCALFE

AN ANATOMY OF GRASSES

Anatomy of the Monocotyledons

By C. R. Metcalfe. Vol. 1: Gramineae. Pp. lxi+731. (Oxford: Clarendon Press; London: Oxford University Press, 1960.) 84*s*. net.

METCALFE AND CHALK is a name as familiar to the botanist as Mrs. Beeton is to the cook and, like Mrs. Beeton, it contains a vast amount of information largely derived from first-hand observation.

The present work is another monument to the skill and indefatigable industry of Dr. Metcalfe, who once again puts plant anatomists and taxonomists in his debt.

The main part of this volume consists of a systemati account of the anatomy of 206 genera and 413 species of grasses which have been investigated by Dr. Metcalfe in the past ten years; to this is added information obtained from the literature about a further 139 genera, so that something of the order of half the genera in the family are considered. Since the genera of grasses, like those of most other families of flowering plants, do not fall readily into a linear sequence, an alphabetical order has, very sensibly, been adopted for this 'histological dictionary' section of the book. The bamboos are regarded as sufficiently distinct in their leaf anatomy to be treated separately after the grasses belonging to other tribes have been discussed. The merit of this arrangement is perhaps open to question, since there are genera, such as *Anomochloa* and *Pariana*, which have many bambusoid features, and the distinction between the panicoid and festucoid types of leaf seems to be almost as clear-cut as that between these types and the bamboos. There might therefore have been something to be said in favour of a completely alphabetical arrangement; this is, however, a minor point.

The introductory chapters on the general morphology of the grass plant and on anatomical characters and their value to the taxonomist provide both a basis for the understanding of the dictionary and an admirable summary and discussion of the detailed information. Dr. Melville is himself very cautious in considering the implications of his anatomical observations for taxonomy, but to one whose knowledge of grass taxonomy is slight and of anatomy even slighter they seem to be of the first importance. Some of them have already been incorporated in taxonomic works by Dr. C. E. Hubbard and others; no doubt the remainder will be speedily utilized.

In this connexion a particularly valuable service is performed in directing attention to genera such as *Danthonia*, which are anatomically heterogeneous, as the desirability of a re-examination of their floral morphology and an investigation of their chromosomes is clearly indicated.

In conclusion, mention must be made of two other excellent features of this book. One is the account of the fairly simple but not generally known methods used in preparing both fresh and dried material for microscopic examination, and the other is the beautiful drawings of the main types of structures described in the text.

One is left with an enhanced feeling of admiration for both the Gramineae and Dr. Metcalfe, and a pleasurable anticipation of further volumes on other families of Monocotyledons.

T. G. TUTIN

SURVEYS IN APPLIED MATHEMATICS

Elasticity and Plasticity

By Prof. J. N. Goodier and Prof. P. G. Hodge. (Surveys in Applied Mathematics, Vol. 1.) Pp. ix+152. 50*s*. net.

Dynamics and Nonlinear Mechanics

By E. Leimanis and N. Minorsky. (Surveys in Applied Mathematics, Vol. 2.) Pp. xii+206. 62*s*. net.

Mathematical Aspects of Subsonic and Transonic Gas Dynamics

By Lipman Bers. (Surveys in Applied Mathematics, Vol. 3.) Pp. xv+164. 62*s*. net.

(New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1958.)

THE great flood of papers in applied mathematics which now pours endlessly through scientific journals from individuals and research groups throughout the world makes it impossible for the practising mathematician to keep fully abreast with new developments, except in some special field in which he is himself working. It follows that surveys of recent work written by authorities in their respec-

tive subjects and intended for the mathematically literate reader who is not a specialist in that subject can be of great value. In particular, they serve to direct attention to ideas and methods developed in one subject which may have useful applications in another. The present volumes are good examples of such surveys. A particularly valuable feature of them is the special attention their authors have paid to recent Russian publications. Indeed, one of the most notable features of these surveys is the great volume and importance of the Russian contributions to most of the subjects discussed.

In the first part of the first volume of the series, Prof. Goodier describes some recent advances in the mathematical theory of elasticity. The most significant of these advances undoubtedly springs from the work of Muskhelishvili, and a great deal of the survey is devoted to his work. His early work on complex potential theory, leading to elegant and comprehensive methods of solving plane problems with prescribed boundary forces or prescribed boundary displacements, is briefly described. This is followed by a rather more detailed, though still condensed, discussion of Muskhelishvili's fundamental work in the theory of complex singular integral equations and the associated Hilbert problem. The solution of this problem using Plemelj's theorem provides a remarkably powerful method of solving mixed boundary value problems. The fundamental theory has of course been available for some years to English readers in J. R. M. Radok's translations of Muskhelishvili's two classical treatises, but there is also a considerable Russian literature on detailed applications to specific problems; the present survey gives a most useful summary of these applications. Other topics briefly dealt with include anisotropic elasticity, thermal stresses, contact problems and wave propagation. The theory of finite deformations is referred to but not described, since an excellent recent account of this is to be found in Green and Zerna's book.

The other part of Volume 1 is a discussion by Prof. Hodge on the present state of the mathematical theory of plasticity. Here the emphasis is rightly placed on the derivation of the fundamental principles and equations of the theory, rather than on methods of solution of specific problems, though one problem, that of a simply supported plate with various types of plasticity, is dealt with in detail as an illustration of the methods at present available; references are also given to a number of other problems. There is a very readable introduction to the general theory, and the postulated properties, such as perfect plasticity, piece-wise linear plasticity, kinematic and isotropic strain-hardening, etc., of various ideal substances are clearly defined. The plastic-flow laws are derived, and the inadequacy of any deformation theory for discussing many problems is emphasized. A short chapter is devoted to Russian contributions, but the very brief descriptions of these prove insufficient, at least to me, to indicate their value and significance.

The second volume of the series is also divided, the first part by E. Leimanis being mainly a discussion of the two celebrated problems in classical dynamics, (i) the motion of a heavy rigid body about a point and (ii) the three-body problem. There is also a chapter on exterior ballistics. Many of the investigations considered can scarcely be described as recent. The solutions of the special cases of the rigid body problem associated with the names of Euler, Lagrange and Kovalevskaya are discussed in some detail, and the investigations of Poincaré, Hess, Schiff and others on the existence of other solvable special cases are described. Almost all recent work relates to special cases, and no significant advance in the theory of the general motion is reported. The situation is not very different for the three-body problem. Little progress towards a general understanding of the problem can be discerned since Sundman's solution of 1912. Indeed, Prof. Leimanis devotes a considerable section to showing that Vernić's recent attempts (1952) to extend the validity of Sundman's solution to triple collisions have not been successful. More satisfactory progress has been made in studies of periodic and asymptotic solutions of both the restricted and the general three-body problem, and Merman's work in recent Russian papers on the problem of capture seems to be perhaps the most significant of recent advances.

In the second part an excellent introduction to the theory of non-linear oscillations is given by N. Minorsky, beginning with and largely based on van der Pol's equation $\ddot{x} + \mu(x^2 - 1)\dot{x} + x = 0$. The important topological concepts introduced by Poincaré, the identification of singular points in the phase plane with positions of equilibrium, limit cycles with stationary motions and so on, are adequately explained, and various approximate methods of solution of the equation $\ddot{x} + x = \mu f(x,\dot{x})$, where μ is small, are described. The radical change in character of the problem when μ is not small is emphasized, and the different methods of approach which have been tried in this case are reviewed. The important work of Cartwright and Littlewood on the conditions for existence of a periodic solution of van der Pol's equation is mentioned, but does not seem to have led to a practical method of solution. Another method of approach is the discontinuous theory of relaxations, analogous to the theory of shocks. This has been developed mainly in the U.S.S.R. by Chaikin, Lochakov and others, and seems at present to offer the most practical tool for applied problems.

In the third volume of the series Prof. Lipman Bers discusses certain mathematical aspects of subsonic and transonic gas-flow theory. He deals exclusively with steady irrotational flows and almost exclusively with two-dimensional problems. He places more emphasis on mathematical concepts and techniques than on specific physical problems, but gives some indication of recent practical methods and results. He devotes much of his discussion to the questions of existence and uniqueness of solution of various problems. Since the governing equations of compressible flow are non-linear and of mixed type, these questions involve some highly sophisticated mathematical arguments, and only recently has much progress been made in finding answers to them. Chapter 1 is a good introduction to the subject and describes the various approximations and modifications of the potential flow equation. Chapter 2 is concerned with the general theory of elliptic equations, quasi-conformal mapping and the theory of pseudo-analytic functions to which the author has himself made important contributions. Chapter 3 applies the results of this theory to subsonic flows. Tricomi's theory of mixed elliptic-hyperbolic equations is discussed in Chapter 4 and applications to transonic

flow are given in Chapter 5. A short appendix is added on numerical methods. This volume is by no means easy to read, but it contains much of interest and value to the applied mathematician.

In conclusion, it may be said that these three volumes, though somewhat uneven in their degree of mathematical sophistication, achieve their purpose of providing a good overall picture of the present state of certain fields of study. They are well produced, and few misprints appear to have crept in, though some were noticed in the third volume.

A. T. Price

NEBULÆ, GALAXIES AND COSMOLOGY

Rival Theories of Cosmology

A Symposium and Discussion of Modern Theories of the Structure of the Universe. By Prof. H. Bondi, Dr. W. B. Bonnor, Dr. R. A. Lyttleton and Dr. G. J. Whitrow. Pp. xii + 61 + 12 plates. (London and New York: Oxford University Press, 1960.) 9*s.* 6*d.* net.

l'Exploration des Galaxies Voisines par les Méthodes Optiques et Radio-Électriques

Par Dr. Gérard de Vaucouleurs. (Collection "Évolution des Sciences", No. 13.) Pp. 156 + 18 planches. (Paris: Masson et Cie., 1958.) 1,600 francs.

Le Nebulose e gli Universi-isole

Da Giorgio Abetti e Margherita Hack. (Biblioteca di Cultura Scientifica, No. 62.) Pp. x + 354. (Torino: Ediziom Scientifiche Einaudi, 1959.) 3,000 lire.

IN the autumn of 1959, the B.B.C. Third Programme broadcast a series of three talks on cosmology followed by a discussion at which the rival theories were debated. The short book *Rival Theories of Cosmology* is a direct outcome of these, the content being substantially the same as that of the talks.

Relativistic theories of the universe are discussed by W. Bonnor in the first chapter. This is followed by an account of the steady-state theory, the case being put by H. Bondi, one of the originators of the theory. Finally, R. Lyttleton explains his idea that the expansion of the distant galaxies may be due to the proton having a slightly greater numerical charge than the electron. The volume contains some good illustrations of galaxies, but the book would have been improved by the insertion of a short chapter on some of the observational aspects relevant to cosmology. The text does not presuppose any detailed knowledge of astronomy or cosmology, and within the limitations which are of necessity imposed by this restriction the ideas are put forward very clearly. The book is recommended to anyone who wishes to be introduced to some of the problems of cosmology.

L'Exploration des Galaxies Voisines has been written by an astronomer who has himself worked extensively in the field concerned. After a brief introduction to the nature and classification of galaxies, the problems of estimating extra-galactic distances are considered in some detail. Subsequent chapters deal with the luminosities, diameters, spectra, colours, rotation and masses of galaxies. In addition, there is a chapter devoted to the information about galaxies which has been obtained by means of radio astronomy. The text is well written in a logical sequence; the plentiful illustrations and diagrams are of a high standard. The author intends to write a second volume in which more general topics such as clusters of galaxies will be treated. There is a dearth of up-to-date books about galaxies, and it is to be hoped that the second volume is of the same standard as this first one.

The work by G. Abetti and Margherita Hack discusses planetary nebulæ, diffuse nebulæ and interstellar absorption before describing some of the structural and kinematic properties of the galaxy. The last chapters are concerned with galaxies in general and the rival theories of cosmology. The scope of the book covers a wide range of subjects which are in some cases rather indirectly connected with each other, and the planning of the volume leaves much to be desired. Despite this criticism, some of the individual description is quite good. The book contains some useful material which is not often found in accounts written for the non-specialist.

J. B. Alexander

VERSATILITY OF VACUUM

Progress in Vacuum Science and Technology

Edited by A. S. D. Barrett. Pp. iii + 160. (London and New York: Pergamon Press, 1959.) 70*s.*

IN recent years vacuum techniques have been introduced into a number of different industrial fields and this book will give the reader a good idea of some of them. The book contains six chapters, each dealing with a particular application and written by an expert in that field. There is also an introductory survey of education in vacuum practice at colleges in the United Kingdom. The contributions have been published as separate articles in the journal *Vacuum*.

Although the book-title includes "Science and Technology", the majority of the chapters are written from a technological rather than a scientific point of view, and are largely descriptive. That on problems in the valve industry does, however, touch on the basic theory more than most. The chapter on the gettering process in receiving valves includes a historical survey of developments leading to the modern type of barium getter. The gas clean-up performance of the latter is given, but the physics of the process is barely mentioned.

The applications of vacuum to metallurgy, fumigation and drying of medical and food products are in complete contrast to valve techniques. These chapters deal with the use of not-so-high vacua on a heavy engineering scale and make interesting and informative reading to those whose knowledge of vacuum is derived mainly from the standard textbooks. The final chapter, on molecular distillation, describes a number of vacuum stills, particularly those of Hickman, who has been largely responsible for recent developments in this field.

A book of this nature is unlikely to be exhaustive, and the most notable omissions are the recent work on ion-pumps and the production and use of ultra-high vacua, which get only passing mention. The book is well produced and fairly free from misprints. Most chapters have an adequate bibliography; that on molecular stills in particular. Thus this book provides a useful survey of the industrial applications of vacuum, in a form suitable for a busy technologist to read.

R. O. Jenkins

A NEW THERMIONIC GENERATOR

By Prof. D. GABOR, F.R.S.

Department of Electrical Engineering, Imperial College of Science and Technology, London, S.W.7

IT has been known since the investigations of Irving Langmuir in the early 'twenties that the thermionic vacuum diode can be operated as a converter of heat into electric power, but with very poor efficiency owing to the minuteness of the currents. In recent years it was recognized that the efficiency could be raised to an economically interesting level if it were possible to compensate the electronic space charge by a sufficiently cheap supply of ions. Cæsium, with the lowest ionization potential of all the elements (3·9 V.) appeared the most promising, all the more as cæsium ions could be produced by the Langmuir–Kingdon effect, that is to say, by contact with the hot surface of materials with a work function exceeding 3·9 V. In the cæsium diode, as developed by R. W. Pidd *et al.*[1], also by K. G. Hernquist[2] and V. C. Wilson[3], cæsium vapour is ionized by contact with a hot electrode which can be either the emitter itself, or a third, hot electrode. The minimum cost per cæsium ion, taking into account the radiation losses of the hot surface, has been estimated as 100 eV., and as one cæsium ion can compensate the space charge of about 500 electrons, theoretically one ampere could be passed through such a diode at a cost of about 0·2 watt. The experimental figures are appreciably larger.

In the new thermionic device an experimental cost figure of 0·05–0·1 watt/amp. has been achieved, moreover not with cæsium, but with argon (ionization potential 15·7 V.) or with an argon–mercury mixture. Using cæsium, the cost could be reduced by a factor of 3–4, but it is doubtful whether it would be worth while to improve the efficiency further at the expense of the useful life of the device, which is likely to be much shortened by the chemically very active cæsium or other alkali metals.

The principle of the new device is illustrated in Fig. 1. The main discharge occurs between an emitter, which can be heated, for example, by flame gases through a ceramic envelope, and a collector electrode. For reasons to be explained later, it is essential to give the collector a large area relative to the emitter; it is therefore realized as a cellular structure. The voltage drop in the main discharge space is of the order of a small fraction of a volt only, so that no ionization or excitation occurs in it, and in operation this space appears dark. All ions are supplied to it from an auxiliary discharge between a gauze or similar perforated structure and an auxiliary anode. In operation a small fraction of the electron current shoots out from the dark plasma in the form of fine electron beamlets through the meshes of the gauze, where an acceleration region is formed, with a drop just sufficient for ionization. Owing to the favourable focusing properties of the electric field, a large fraction of the ions thus formed returns through the meshes into the main discharge space. The flow of electrons and ions is illustrated in the left half of Fig. 1, but only schematically, just to illustrate that only a small fraction of the emitter current goes into the auxiliary discharge, while a large fraction of the ions find their way to the cathode. There is some experimental evidence that this is aided by reflexion of the slow ions at the walls of the collector, because increasing the surface of the collector by a cellular structure had a remarkably small influence on the auxiliary discharge required to maintain a certain emitter current. The question mark in the reflected ion path indicates our almost complete ignorance on the subject of the reflexion of very slow ions at surfaces.

It is very essential for the operation of the device that the auxiliary discharge has a positive characteristic, as only this enables thousands of tiny discharges in the meshes to operate in parallel. This is true for all inert gases and also for mixtures of argon and mercury up to a certain proportion of mercury. (For example, 2 mm. argon, with mercury saturated at 80° C.) In pure mercury the elementary discharges tend to have a negative characteristic, and instead of the operation as illustrated one then obtains an arc through a single mesh. In order to make the operation economical the meshes are made sufficiently wide so that the drop in the accelerating region exceeds the ionization potential only a little (80–120 wires per inch). As the anode drop at the auxiliary anode is negative, the total drop in the auxiliary discharge can be appreciably less than the ionization potential, for example, 10 V. in argon, only 7·5 V. in an argon–mercury mixture. The ions are therefore rather slow when they shoot through the gauze, and are slowed down further by collisions with gas molecules, so that they have little more than the gas temperature by the time they reach the cathode.

According to I. Langmuir's theory[4], slow ions coming from a plasma will compensate optimally the space charge of the electrons, emitted by a hot cathode, if the ion current is a fraction $\sqrt{m/M}$ of the electron current, where m is the mass of the electron, M of the ion. This ratio is 1 : 272 for argon, 1 : 494 for cæsium, 1 : 607 for mercury. Though Langmuir's theory was an excellent qualitative guide in the experiments, it might require some quantitative revision because the auxiliary currents in argon were in some experiments as small as 1/100 of the emitter current. Even if all the power in the auxiliary discharge were converted into ionization, this would give only about one ion for 160 electrons, and as the ionizing efficiency was certainly much short of 100 per cent and as some ions must have been lost in the gauze and at the walls, it appears very likely that the ion : electron ratio can be, in fact, better than Langmuir's optimum, again suggesting that there is some reflexion of slow ions.

The picture of the discharge derived from our experiments is illustrated in the right half of Fig. 1. The dark discharge space is filled with a dense plasma of remarkably small electron temperature. At low currents this is only a few hundred degrees in excess of the emitter temperature, indicating that the cathode drop is a few hundredths of a volt only, rising to a few tenths at large currents. As the current density can be of the order of an amp./cm.², the cathode sheath thickness must be of the order of

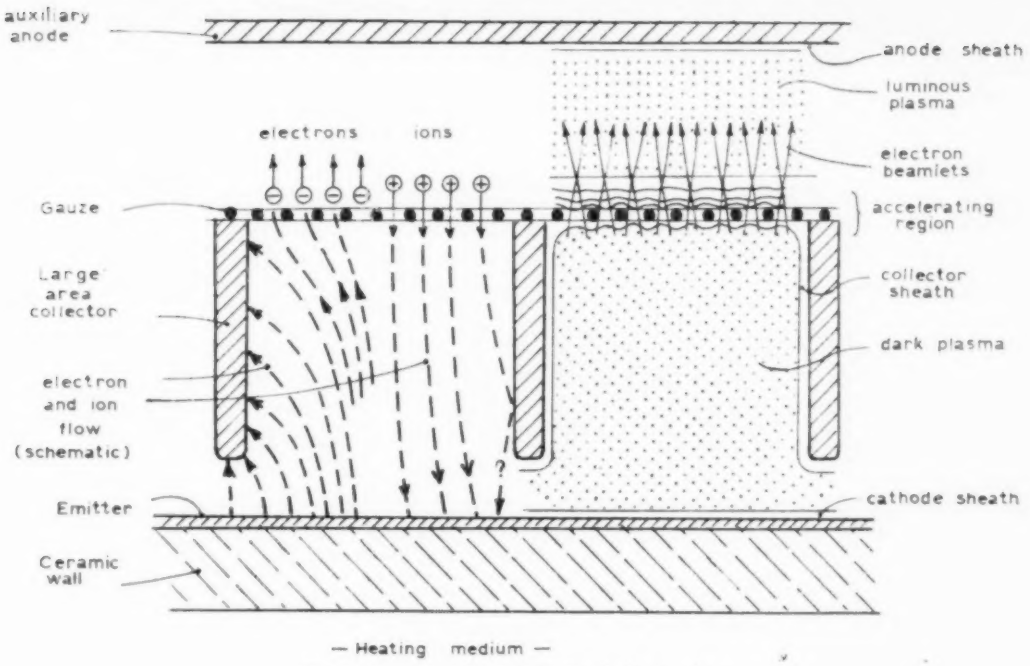

Fig. 1. Schematic section through thermionic generator

1/2. At small currents the plasma has a practically uniform potential; at higher currents a gradient develops. It is a fortunate circumstance that owing to the Ramsauer effect the cross-section of argon to electrons with energies of the order of a few tenths of a volt is very small, but even if it were zero the resistivity of a plasma, as estimated by Gvosdover[3] and by Spitzer[4], is not negligible. At the collector there is a negative drop in all circumstances which we have investigated, and this can be larger than the cathode drop, so that the total voltage drop in the gas space can be negative.

These conditions are further illustrated in Figs. 2 and 3. Fig. 2 is a diagram of the potential from terminal to terminal. As a typical example the emitter work function $\varphi_{em.}$ may be 2·5 V., the collector work function $\varphi_{coll.} = 1{\cdot}0$ volt, giving a nominal terminal voltage of 1·5 V. per element. Fig. 3 shows the voltage-current characteristics of the device, theoretically derived but well confirmed by experiments. The theory starts from the assumption that at small currents the discharge space is filled with a uniform, equipotential and, as regards the electron temperature, isothermal plasma. Consider first the case of zero potential difference between emitter and collector. In that case the same random electron current flows from the plasma to equal areas of the emitter or of the collector. The current density at the collector is equal to this random current, while at the emitter it is the difference between the saturated emission and the random current. It follows at once that at $V = 0$ the current is a fraction of the saturated emission current equal to the ratio of the collector area to the total area, that is to say, emitter plus collector. In the diagram it has been assumed that the collector area is three times the cathode area, hence at $V = 0$ the current is 3/4 of the saturation current. The saturation current is limited either by the thermal emission of the cathode, or by the ion supply. By Langmuir's rule the ion-limited current is $\sqrt{M/m}$ times the ion current, and will be proportional to it until thermal saturation is reached. This has been well confirmed by experiments, because it was found that the saturation currents were proportional to the currents in the auxiliary discharge, in any event at low values of the current. With oxide cathodes at high auxiliary currents there is no sharp limiting current because at ion supplies exceeding Langmuir's ratio there will be a non-zero electric field at the emitter, and in composite cathodes field-assisted emission is relatively important.

The same model of a uniform, equipotential and isothermal plasma applied to non-zero values of V gives a current characteristic $I(V)$ in the shape of a hyperbolic tangent function, with a subtangent $4kT/e$, where T is the electron temperature. This was verified, and the value of T agreed well with that obtained from Langmuir probes. At low currents, T was found to be only slightly larger than the emitter temperature. At currents large enough for the plasma resistance to become noticeable this model ceases to apply because the plasma will no longer be equipotential. A good qualitative insight can be obtained by using Steenbeck's principle, according to which the potential profile and the electron temperature will adjust themselves in such a way as to make the total heat dissipation at given current a minimum. The heat dissipation per unit current is $V + 2kT/e$, the second term being the kinetic energy which the electrons give up to the collector, and the electron temperature T must be such as to make this a minimum. As by Spitzer's law the plasma resistance is proportional to $T^{-3/2}$, the electron temperature will increase with rising current, ultimately with the 2/5

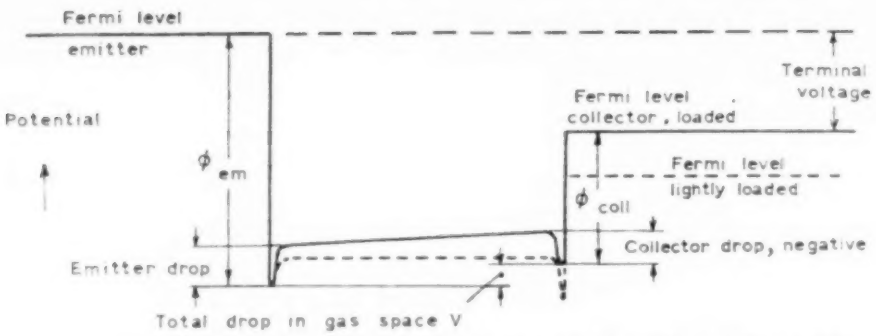

Fig. 2. Potential diagram. At light loading (broken lines), the plasma has a uniform potential; at heavy loading (continuous lines), the effect of plasma resistance becomes noticeable

power of the current density. This is qualitatively illustrated in Fig. 3, where the base $4kT/e$ broadens with increasing current. Experimentally we have observed an increase of kT/e from 0·11 V. at small currents, to 0·25 V. (2,900° K.) at the largest densities investigated.

This is one of the effects of large currents. The second is a shift in the characteristic, owing to the gradient in the plasma. This, too, is illustrated in Fig. 3. At the point where $I = 0{\cdot}75\ I_{max.}$, which would correspond to $V = 0$ if the plasma were equipotential, the characteristic at higher current densities is shifted to the right by an amount V, which is the drop in the gas space. To obtain an idea of this drop note that Spitzer's law gives a plasma resistivity of the order:

$$\rho = 1{\cdot}0\ (T/1{,}000)^{3/2}\ \text{ohm. cm.}$$

At the low electron temperatures with which the thermionic converter operates this is quite appreciable. Even at $T = 2{,}900°$ K. it is still 0·2 ohm. cm. Thus, if we had a plane emitter faced by a plane collector at a distance of 1 cm., we should have at 4 amp. cm.$^{-2}$ a drop of 0·8 V., which is far too large

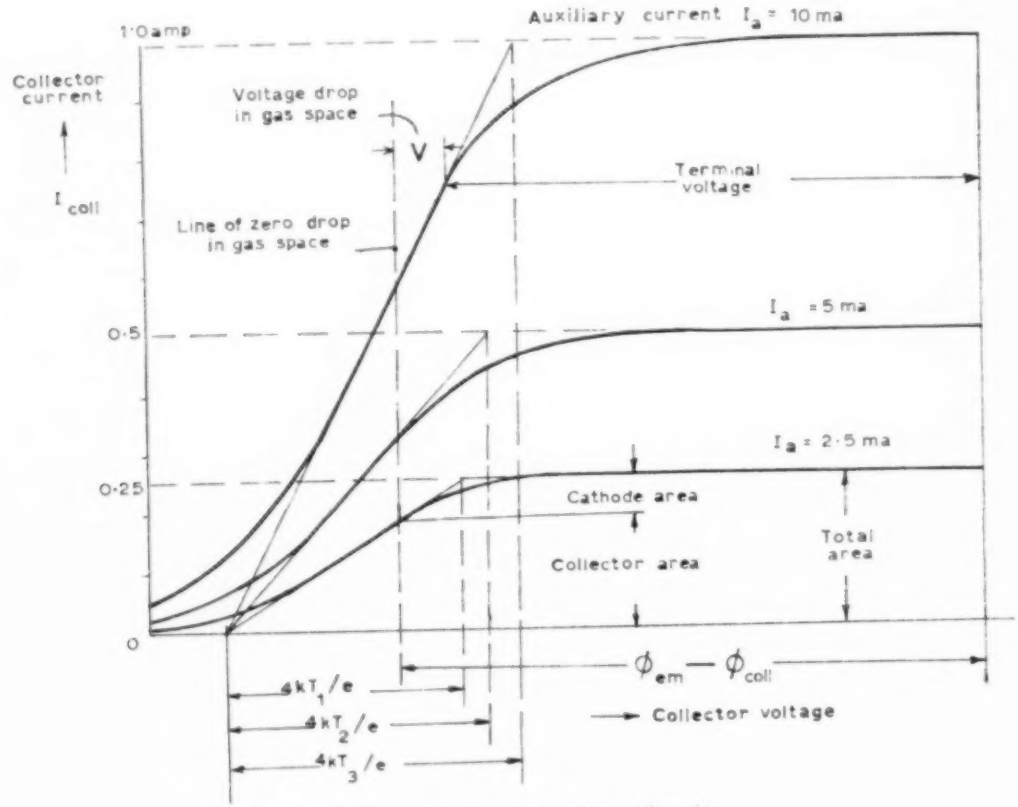

Fig. 3. Current-voltage characteristics, schematic

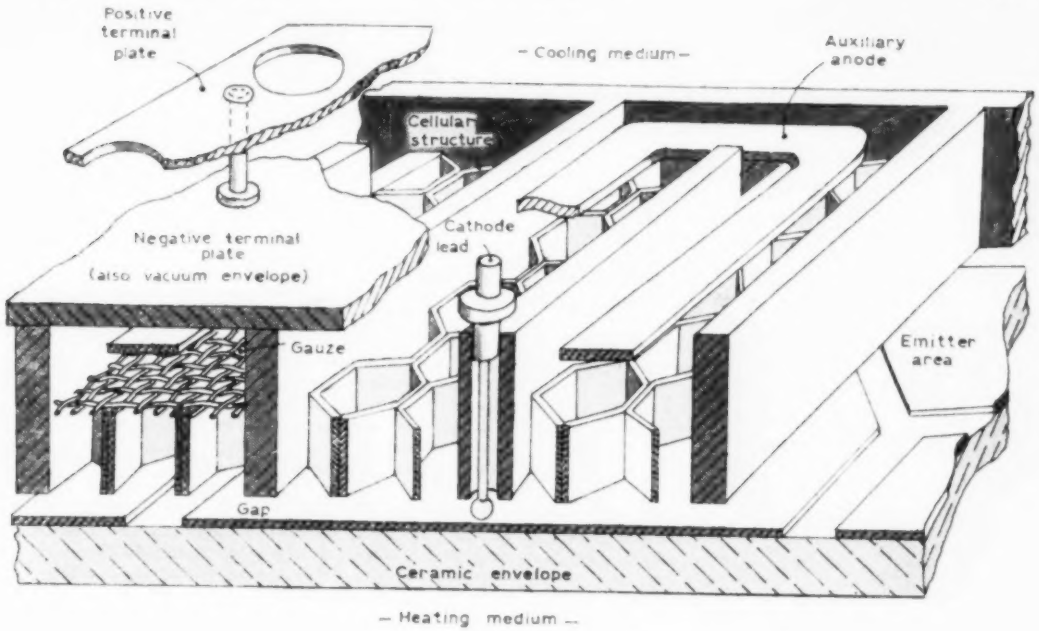

Fig. 4. Thermionic generator element

to be tolerable. This has an important consequence for an economic design. It was shown previously that in order to reduce the voltage drop, the collector area must be large relative to the cathode area. It is seen now that in addition we must also reduce the absolute dimensions of the emitter-collector assembly.

Fig. 4 shows a design of a thermoelectric generator in which this is taken into account. The collector consists of a cellular metal structure, of a material with good heat conductance, interspersed with bars of sufficient cross-sections to conduct the heat without a large temperature-drop to a terminal plate, which is immersed in the coolant. The cells have small dimensions, say 3–5 mm., and they are within a small distance, say 1 mm. from the face of the emitter, so that the plasma resistance is that of a pair of parallel plates at about 2 mm. distance. This is sufficient for current densities of the order of 4 amp./cm.^{2}; for higher densities the dimensions ought to be further reduced. It is seen that the fineness of this 'microstructure' does not prevent the realization of large units.

A metal gauze is applied to the top of the cellular structure, separating the auxiliary discharge space from the main space. This second space contains a meandering auxiliary anode. It has been found that a single auxiliary discharge space is preferable to one broken up into smaller units, as it ensures that the discharge will spread over the whole surface of the gauze.

While most prime movers improve in efficiency when they are scaled up, large thermionic generators beyond a certain size suffer from a grave disadvantage. This is the self-magnetic field of the generated current, which tends to prevent the emission by returning the electrons to the emitter. One can reduce this somewhat by admitting the currents not at one point but evenly over the periphery of the device, but only up to a certain limit. As an example, let 25 gauss be the limit of the magnetic field parallel to the emitter surface which one can tolerate. Such a field is produced by 20 amp./cm. With a current density of 4 amp./cm.^{2} this limit is reached in a square of 20 × 20 cm., at a current of 1,600 amp. If one makes the unit larger the current will not increase, because the emission will be cut off beyond the critical square. Larger units must consist 'magnetically' of sub-critical units. One way of achieving this is shown in Fig. 4. The emitter area is divided into hexagonal sub-areas, each with its own cathode lead in the centre. If these are small enough the loss by magnetic fields can be made negligible. For example, if each sub-unit supplies 100 amp. and has an area of 25 cm.^{2}, the critical area around the lead in which the magnetic field is more than 25 gauss has a radius of 0·8 cm. and an area of 2 cm.^{2} only, that is, 92 per cent of the emitter area is utilized. An advantage of this design is that each cathode lead acts also as a mechanical support for the ceramic envelope against the atmospheric pressure. Moreover, one finds that if these leads are made, for example, of tungsten or molybdenum, of such thickness as to present the optimum compromise between ohmic drop and heat conduction, they will be flexible enough to follow the differential thermal expansion between the emitter and the collector structure. All cathode leads are connected with a positive terminal plate which is perforated and immersed in the coolant. Such units can be made in any size, and they need not be necessarily plane.

The efficiency of thermionic generators has been calculated by several authors, in particular by J. M. Houston[7]. It is

$$\eta = \frac{\varphi_{em.} - \varphi_{coll.} - RI - (\text{drop in discharge}) - (\text{cost of ions in W./amp.})}{\varphi_{em.} + 2(k/e)T_{em.} + (\text{heat conduction amp.}) - (\text{radiation/amp.})}$$

RI is the internal ohmic drop. The optimum compromise between this and heat conduction is usually at $RI = 0{\cdot}05$–$0{\cdot}1$ V. The conditions which favour a small voltage drop in the discharge and reduce it to 0·1–0·2 V. or less have been already discussed, and it has been mentioned at the beginning that the cost of ions can be made as low as 0·05–0·1 V. in the present device. The most important parameters for good efficiency are therefore the work functions $\varphi_{em.}$ and $\varphi_{coll.}$ and the radiation per ampere emission. The heat conduction through argon at about 2 mm. pressure plays a small part in the losses. The work function of the collector must be evidently made as small as possible. It can be reasonably expected that it will be possible to reduce it to 1 V. This leaves us with finding a suitable compromise between the emitter work function and the radiation loss per amp. current. The best compromise depends on the emitter temperature. If this is given, one has the choice between a larger $\varphi_{em.}$ giving a higher terminal voltage but smaller currents and thereby larger radiation loss per ampere, or a smaller $\varphi_{em.}$ with smaller radiation losses. At emitter temperatures of 1,500°–1,800° C. the choice is largely in the region $\varphi_{em.} = 2{\cdot}3$ V., and working out examples with existing emitter materials one finds that the advantage is on the side of the lower work functions. These give not only better efficiencies but also higher power densities, that is, better utilization of space. With present cathode materials one can contemplate efficiencies of the order of 20–30 per cent and power densities of the order of 4–6 kW./sq. ft.

It is a unique advantage of the new device that it allows the direct generation of alternating current. The device becomes at once non-conducting if the auxiliary discharge is extinguished, and can be made conducting in a fraction of a millisecond by re-striking it. Thus, if one takes two of these devices and connects them in push–pull over a transformer as output, so that they will send currents into the transformer alternatingly, one obtains alternating power. One can supply this to an a.c. network by deriving the small auxiliary power from the mains in synchronism with it. The efficiency in a.c. operation is somewhat smaller than with d.c. because heat conduction and radiation go on also during the non-operative half-cycle, but the reduction in efficiency (say from 30 to 22 per cent) might well be outweighed by the gain in the cost of the plant.

Though the investigations of the gas discharge in the new thermionic device are not yet closed, these phenomena are now sufficiently understood to form the basis for the design of practical generators—given suitable materials. Further research must be directed towards the three problems in material technology presented by this or any other thermionic converter. The first is a cathode material with 2–2·5-V. work function, with small radiation emissivity, capable of supplying 4 amp./cm.² or more at temperatures in the region of 1,200°–1,800° C. The second is a suitable collector with high reflectivity and low work function. In a self-contained generator in which the coolant temperature is, say, 100° C., this ought to be about 1 V. In a generator used as a 'topper' for a steam turbine, with the coolant at 5–600° C., it can be 1·5–1·8 V., and there exists a fairly wide range of suitable materials. Such a converter would amount to a boiler which turns a part of the fuel energy directly into electric power, the rest into steam.

The third problem, probably the most difficult, is that of a ceramic envelope impervious at 14–1,800° C., capable of operating for long times when exposed to flame gases and with a high thermal shock resistance. This last problem would not arise in one line of possible applications, namely, as a converter in an atomic reactor in which the nuclear fuel could be included in the envelope. This application, however, will not mature until it is proved that fuel elements can operate at such high temperature, and do not contaminate the emitter, the collector and the gas with fission products. A small amount of gas contamination, as well as some measure of gas transmission in the ceramic envelope, can be dealt with by titanium pumps or the like, which eliminate chemically active contaminants, but not argon or other inert gases.

Provided that these problems can be solved satisfactorily, combining a low cost with a long life, there is a wide field of potential applications for thermionic generators, in supplying d.c. power for electrochemical plants, for traction, for small self-contained generator units, and for improving the efficiency of large steam or nuclear power plants.

My thanks are due to Mr. H. A. Fatmi, who has carried out the experimental work, and to the National Research Development Corporation, which provided the financial support.

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THE MARITIME UPLANDS OF BRITAIN: INVENTORY AND PROSPECT

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THE alleged equability of British climate is a notion derived not only from a traditional consideration of exclusively mean meteorological data but also from the fact that the vast majority of the major synoptic meteorological stations of Britain are situated at low elevations (see Fig. 1). It is well known that weather, climate and ecological potential deteriorate with increasing altitude in the British Isles, but the remarkably rapid rate of deterioration, even for a maritime climate, is much less publicized. If, for idealized maritime and continental sites (Fig. 2), horizontal lines A (low-level) and B (high-level) for the former, and lines A' (comparable low-level) and B' (comparable high-level) represent growth thresholds (for example, 42° F.) crossed upwards in spring and downwards in autumn

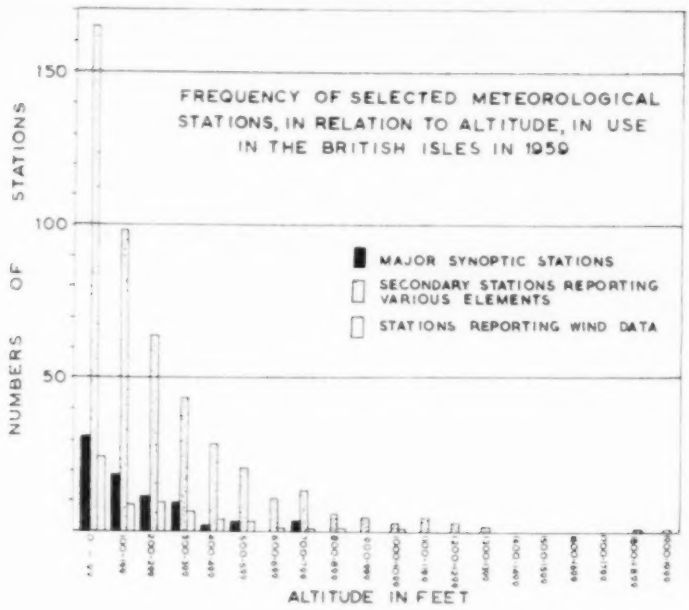
FREQUENCY OF SELECTED METEOROLOGICAL STATIONS, IN RELATION TO ALTITUDE, IN USE IN THE BRITISH ISLES IN 1959
MAJOR SYNOPTIC STATIONS
SECONDARY STATIONS REPORTING VARIOUS ELEMENTS
STATIONS REPORTING WIND DATA
NUMBERS OF STATIONS
150
100
50
ALTITUDE IN FEET

Fig. 1

by the mean monthly temperature curves, then the vertically shaded and stippled areas represent the relative amounts of growth potential at each site and elevation. Clearly, the maritime site, despite its earlier and longer season, has a lower growth potential, which is reduced rapidly with elevation. The continental site, however, despite its later and shorter season, has a greater growth potential which is reduced much less rapidly with elevation. It follows that agricultural limits, tree-lines, snow-lines, etc., occur at much lower elevations at maritime, compared with continental, sites.

This sharp ecological gradient[1] is the expression of decreasing temperatures, especially maximum temperatures, and of increasing rainfall, derived more from the elevation and modification of frontal structures than the simple rise of moist air streams. Increasing cloud cover and persistence, relatively low-cloud bases, high humidities and the liability to mist or fog accompany the increasing rainfall. Complementarily, evaporation (when it is possible) and sunshine amounts are reduced to a minimum. Frost incidence, snow-fall, snow-cover[2] and wind-speed[3], with few exceptions, also increase with altitude. All these trends imply a progressive, exceptional rate of deterioration of meteorological and ecological conditions with altitude in Britain.

The techniques of pollen analysis and carbon-14 dating have enabled a reconstruction of the vegetation chronology since the end of the last major glaciation (about 12000 B.C.). Tundra was eventually succeeded first by birch and pine forests and then by mixed, deciduous oak woodland which, by the post-glacial climatic optimum (6000–2000 B.C.), attained elevations substantially higher than the 2,000-ft. contour. During the early Mesolithic (8000–6000 B.C.), upland Britain was extensively covered with birches and pines under a relatively dry, continental 'Boreal' climate. From the late Mesolithic (5000–2800 B.C.) through to the Neolithic and the end of the Bronze Age (about 500 B.C.), thick, deciduous woodland containing much oak and alder dominated at first under a warmer, oceanic, 'Atlantic' climate from about 5000 B.C. to about 3000 B.C., and later under the drier régime of the 'Sub-Boreal' phase from about 3000 B.C. to about 500 B.C. Afterwards, the 'Sub-Atlantic' phase (about 500 B.C. *et seq.*) witnessed a resumption of a moister climate and progressively slow, then rapid, deforestation of upland Britain by man, and the creation of the moorland landscapes we know to-day.

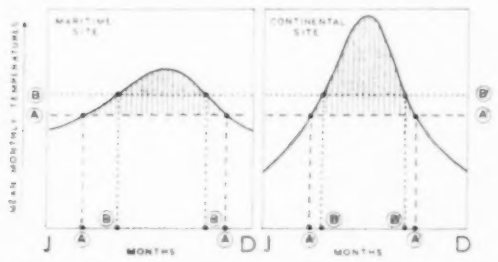

Fig. 2. Diagrammatic comparison of mean temperatures and growing season at maritime and continental sites

Some of the more striking features of the 8,000 years of the post-glacial period are embodied in contemporary soil profiles in upland Britain. The deciduous forest climax was longer and more potent than the preceding birch and pine forests, and promoted the development of deep brown earths. The qualities of colour and texture in the *B* horizons of many contemporary hill soils at present under an incongruous grass vegetation may be attributed to this period. The thick mantle of hill peat developed on typically flattish or gently sloping sites accumulated in particular during the oceanic 'Atlantic' phases. On the other hand, the contemporary semi-natural moorland grasses have formed dense, matted root layers, forming the familiar 'organic-top' of many hill soils, below which a bleached A_2 horizon, greyish in colour, is characteristic. The local development of iron pans or organic pans at the top of the *B* horizons may create impedance within the profile, as evidenced in the mottling of the lower section of the A_2 horizon. These features are expressed in the peaty-gley-podzol which is the most common soil in upland Britain. They are the creation of past vegetations and climates as well as contemporary vegetation and climate, and of past, as well as present, usages by man and his grazing animals.

It is surprising that man's continuous, if extensive, use of the hills in Britain has not facilitated more intensive inquiry into the hill environment itself. The upland soils have been least modified by agriculture and could provide more direct evidence of post-glacial pedogenic processes than their intensively cultivated lowland counterparts. Yet the latter take precedence over the former in the programme

of the Soil Survey. Again, the semi-natural upland vegetation is regarded as something to be improved and 'forced' for grazing purposes—rather something which, in fact, has been degraded by grazing. Detailed vegetation maps of the uplands of Britain scarcely exist. The upland climates of Britain, except for individual short-period investigations, remain taken for granted and often incompletely appreciated. The relatively low contemporary economic value of the uplands of Britain has been a major factor in this neglect. Once areas of pioneer colonization by primitive man, these uplands have now become depopulated and devalued by modern man. The agricultural lowlands and the coalfields have claimed priority in geological and pedological surveys[4]. The popular comment, "all our vegetation has gone" has perpetuated the almost peculiarly British notion that we live in a conquered environment virtually emancipated from the extremes of Nature. In the hill areas nothing could be further from the truth. Economists to-day repeatedly insist that the hills should be left to water conservation, afforestation, national parks and nature reserves. Hill soils and hill climates have been ecological proof of this doctrine for thousands of years. However, the relegation of sheep-farming and promotion of water conservation and afforestation requires careful and comprehensive planning, which should consider ecological, pedological and sociological argument, in addition to the purely economic considerations.

Cattle depopulation and the gradual disappearance of older sheep from upland Britain have caused a decline in intensity of grazing in recent decades. Consequent regeneration, especially of bracken, has proceeded at locally alarming rates. Bracken is apt to colonize the deeper, non-impeded brown earths which are normally the most productive and versatile soils on the slopes; areal loss is thus coupled with loss of good land. Much Welsh *ffridd*/*oedd* has been transformed into bracken fields dotted extensively with scrub oak, hawthorn and dwarf gorse. The monopolistic, selective grazing by sheep has allowed species such as *Nardus* and *Vaccinium* to dominate many associations at one time richer, for example, in *Molinia* and *Agrostis*. Heather monocultures (for example, in parts of the Scottish Highlands and on the Llandegla Moors in north-east Wales) induce relatively strong soil-podzolization and confine land use to extensive sheep grazing, usually by Scottish blackface.

The dairying revolution of the period *circa* 1933–52 is still registering in remote parts of the uplands of Britain, affording modern evidence of the traditional delay in cultural response which has characterized the Highland Zone of Britain since the earliest times. Some mid-altitude farms have recently introduced milk production, provided they were located within, or within reach of, the catchment of a milk lorry. Many what may be termed 'natural rearing farms' have been modified in this fashion in response to the temporary and, in many ways, excessive economic provocation embodied in the attractive marketing and price facilities and the regular income offered by the Milk Marketing Board. At the same time, sheep farmers face the annual problem of the high cost of wintering their flocks on lowland farms. The comparatively short-term economic and political arguments which initiate these trends and problems should always be qualified by the excessively sharp decrease in flexibility and adaptability of farming systems, and of farms with large proportion of 'hill', with increasing altitude in the maritime uplands. Also, the law of systematic and regular integration between hill farm and lowland farm is herein revealed and is inescapable.

Relatively recent allocations of hill land have been made to the Forestry Commission, to water and electricity authorities, to the National Parks Commission, the National Trust and the Nature Conservancy, to the Army and to the British Atomic Energy Authority.

To what extent the introduction of conifers (for example, since 1927 in Dovey Forest) on partially podzolized soils has induced further podzolization is debatable. Preliminary evidence[5] indicates that little, if any, perceptible degradation has taken place, in particular in Wales, where parent materials in general do not possess an adequate combination of extreme porosity and acidity, as for example occurs in the Barton Sands of the New Forest, where a period of only twenty-five years under conifers has been enough to create advanced podzolization[6]. Afforestation, on the other hand, has helped to check rural depopulation and has provided good, new access roads for many hill farms.

The economic priority claimed by water and electricity authorities in the creation of reservoirs and impounding of water must be assessed against what often amounts to the effective elimination of the antecedent forms of land usage. Planted trees may share the slope with sheep, trees and sheep may occupy land within a national park, but a flooded valley must lose not only its trees and its sheep but also its land as a whole, good, bad or indifferent, and its settlements, people and history. The valley, as it were, dies. But a new lake, a new landscape is created, and miles away a new industry expands and flourishes.

Extensive sections of hill country in Britain have been declared as national parks and provide extended scope for tourism, the industry which to-day can claim one of the largest individual incomes in the country. Tourism, together with water storage, represents potentially one of the most profitable uses which can be made of the uplands of Britain, provided modernized accommodation and hostelries of the right calibre can attract an adequate range of tourists. This will require continual improvements in communications, especially by road.

More limited hill areas have been taken by the Nature Conservancy and the National Trust, and afford opportunities for studying the relation of plant regeneration to soil, slope and climate. Evidence derived from such an investigation will confirm the ecological law that, with increasing altitude in Britain, it becomes progressively—and soon remarkably—less profitable to create artificial soil conditions to introduce lowland species of plants or plants bred specifically to cope with more rigorous environments. Whatever success is achieved on a re-seeded hill, grazing is notoriously short-lived and uneconomical.

The availability of large areas of unpopulated hill has among other factors favoured the creation of army training camps and, very recently (1960–61), the establishment of nuclear power stations, such as that at Trawsfynydd in Merionethshire.

Hill farming leans on Government subsidies. Forestry represents a long-term Government investment. Forestry, in the long run, is relatively more profitable per acre and employs more men per acre[7] than hill-farming which, for the most part, retains

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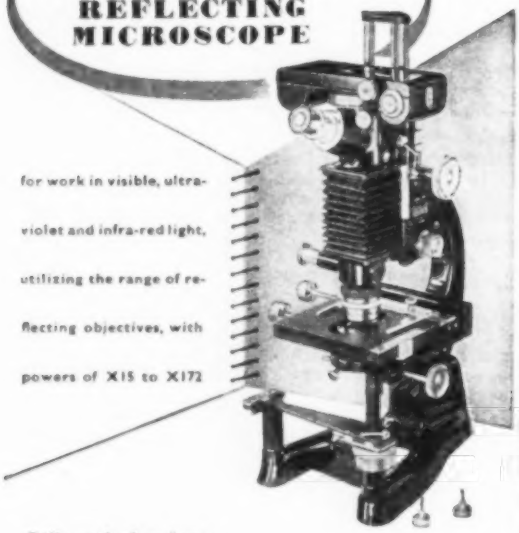

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the better land on the lower slopes and plateaux and valley bottoms, permitting plantation on the higher, or more exposed, or more steeply sloping, ground. It is reasonable to argue that, given equal status in land allocation, forestry would be even more profitable than hill-farming and on lower ground even more profitable still. But sheep farms are indigenous, as it were, to the hills; the plantations are intrusive. Forestry can exploit the more remote hill land more effectively, but at the cost of a longer journey-to-work. The sheep farm (except for certain types of fragmented holding), is a more self-contained labour unit with traditional, external contacts for marketing and social excursions. Rearrangement and amalgamation of holdings might be advocated to promote, rather than reduce, these contacts. New villages created *ab initio* by the Forestry Commission pass through a very difficult formative period until the second generation, born in the village, becomes adult. It is wise to extend old villages where a traditional community spirit already exists. Under-grazing by sheep has allowed extensive regeneration and loss of hill grazings, and soils undisturbed under matted grass (and derived organic top-layers) for many years become badly aerated and deficient in moisture in dry spells. Re-introduction of store cattle on the hills to graze with the sheep would help to reduce degeneration of grazings. In contrast, preliminary treatments for tree-planting often include deep ploughing, especially when drainage is poor and, although catchments may become temporarily flooded by the improved drainage, the mechanical disturbance and overturning of the soil breaks up the root mat, improves aeration and brings relatively richer *B*-horizon material to the surface. On steep slopes, however, there is a danger that erosion might occur.

The implication of the foregoing paragraphs is that whereas forestry must in Britain claim economic priority over hill-farming virtually to the extent of being permitted access to some of the better land, the deep-rooted traditions of the countryside and its settlement pattern remain centred on its sheep farms and associated hamlets. Also, the implication is that the two can be usefully integrated rather than being allowed to compete; this point will be developed later.

Clearly, the future expansion of industry in Britain and the maintenance of a national economy based on adequate exports will demand more extensive and more efficient harnessing of the water resources of the country, in particular in the Highland zone. Thus, water storage both for industry and for power development must claim the highest priority in the planning of upland land use. On the whole, the afforestation of catchments of reservoirs might be favoured, causing further shrinkage of areas devoted to hill-farming. Sheep are tolerated more on the catchments than cattle as a rule; thus the mixed grazing advocated above on ecological grounds is not always practicable. The relatively small areas taken by the Nature Conservancy, the National Trust, the Army and the Atomic Energy Authority are fully justified in terms of urgent national requirements, and the functions of those organizations. The larger national parks are equally justified on grounds of amenity and tourism. It should be asserted, however, that sites of supreme ecological interest or natural beauty should, so far as possible, not be adopted either for military training or for the establishment of nuclear power stations.

In summary, the general order of priority of land use in the uplands of Britain, according to contemporary economic trends, would be as follows: (1) water conservation for industry and for power; (2) afforestation, including the establishment of shelter belts; (3) stock-farming, including store cattle as well as sheep on reorganized amalgamated holdings.

Within this broad framework of priorities, the local priorities concerning (*a*) tourism, both coastal and rural, winter and summer; (*b*) nuclear power stations; (*c*) military and conservation allocations seem justifiable, provided ecological and aesthetic arguments are satisfied.

The creation of a reservoir eliminates all other forms of land use from the site. Cattle-grazing is not encouraged on the catchment of the reservoir, where afforestation is favoured rather than sheep grazing. Forestry, claiming slight relative economic priority, may in the future deserve better hill land at the expense of the adjacent sheep farms, and even some lower ground at the expense of lowland farms. Afforestation blocks may reduce the internal mobility of a sheep farm. The forests may have been sited long distances from existing settlements, where there is competition for a limited and ageing labour force. New settlements vie with old settlements for people and social and religious privileges. External (for example, non-Welsh) forces in the form of new jobs and new workers compete with local tendencies to conservatism and conventionality. How can a declining population maintain cultural integrity and assimilate incoming cultural influences without suffering dilution? How can old and new elements in the labour force continue to tolerate life in remote hill areas, when for many individuals it probably hangs at this moment by the slender penetrating thread of the television screen? How long will it take for the influence of the progressive emancipation of generations of women and mothers to encompass all rural areas? How long will parents and local authorities tolerate an educational system which permits variety in local opportunity for children at the age of 11+ years and demands the steady annihilation of the country schools within the devouring, centralizing orbit of large, new, cumbersome secondary schools to which rural children are 'exported' and 'imported' daily over many miles? How can this picture of all-round competition and collective decline be reconciled?

Reconciliation must lie in integration, which necessitates some degree of planning. The location of water storage schemes should be arranged so as to create a minimum of dislocation of existing settlement and economy. The Forestry Commission should be encouraged to continue to plant above the commercial tree-line for shelter purposes on sheep farms and allowed to experiment on lower ground to ascertain possible increases in yield. Sheep farmers should be educated to accept some degree of reorganization and amalgamation of holdings as the price to pay for greater economic and social security. The re-introduction of store cattle would give more flexibility to the farming system. The occupiers of the smaller holdings should be encouraged to take part-time jobs in the Forestry Commission which should be made available in its programmes of future expansion. For time immemorial the earlier inhabitants of the hills combined several tasks, for example, domestic craft, mining, sheep farming, cattle farming, and the basis of their success was co-operation, especially during the vital summer months when the

mountain pastures were systematically grazed. These ancient laws of job combination and co-operation probably still apply even in the different economic world of to-day. New settlements should be representative of all the labour force and not confined to one type of worker, for example, forestry employees. Moreover, they should be attached to, or be within easy reach of, existing settlements and amenities. Improvement of communications, achieved by the Forestry Commission, for example, should go hand in hand with other forms of planning land use, making the economy more efficient and attracting a bigger and more versatile tourist trade.

These anticipated plans imply change in one form or another. The view that rural cultures (for example, Welsh culture) should not tolerate contamination should be weighed against the inevitability of the economic decay that must accompany their continued isolation.

This commentary owes much to a symposium on "Hill Climates and Land Usage, with special reference to the Highland Zone of Britain", convened by the author in Aberystwyth in March 1960. A memorandum including ten papers was compiled, based on the discussion, and circulated as *Mem.* No. 3, Aberystwyth. Grateful acknowledgment is also made to Prof. Gordon Manley for many valuable criticisms.

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NEWS and VIEWS

The Royal Society of Edinburgh : Awards

The following awards have been made : *Makdougall-Brisbane Prize* (1958–60), to Mr. Albert G. Long, Duns, Berwickshire, for several papers on palæobotany published in the *Transactions* of the Society during the period of the award. *Dr. W. S. Bruce Memorial Prize* (1960), to Mr. J. MacDowall, Meteorological Office, London, for his work in the fields of Antarctic meteorology and geomagnetism and as leader of the Royal Society of London Expedition to Halley Bay, 1958 (this Award is made jointly with the Royal Physical Society and the Royal Scottish Geographical Society). *Bruce–Preller Lecture* (1961) : Dr. V. A. Eyles, formerly H.M. Geological Survey, London and Edinburgh, has been invited to deliver the Bruce–Preller Lecture, 1961, at the ordinary meeting of the Society on June 5.

New Fellows

The following have been elected Fellows of the Royal Society of Edinburgh : Dr. F. Alexander, reader in veterinary pharmacology, University of Edinburgh ; M. Campbell, secretary, Department of Agriculture and Fisheries for Scotland ; Dr. A. J. O. Cruickshank, reader in electrical engineering, University of St. Andrews ; Prof. R. B. Dingle, professor of theoretical physics, St. Salvator's College, University of St. Andrews ; Dr. P. S. Farago, senior lecturer in natural philosophy, University of Edinburgh ; Dr. P. B. Fellgett, principal scientific officer, Royal Observatory, Edinburgh ; K. B. Fraser, senior lecturer in botany, University of Aberdeen ; Prof. A. Haddow, professor of experimental pathology in the University of London, and director of the Chester Beatty Research Institute, London ; W. T. Harry, lecturer in geology, University of St. Andrews ; Prof. A. W. Hendry, professor of building science, University of Liverpool ; Prof. J. S. S. Inglis, professor of animal husbandry and preventive medicine, University of Glasgow ; Dr. H. Lister, lecturer in polar studies, University of Durham, Department of Geography, King's College, Newcastle upon Tyne ; D. Lowe, horticulturist, Elvingston, Gladsmuir, East Lothian ; Dr. R. C. Mackenzie, head of the Department of Pedology, Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen ; B. Noble, senior lecturer in mathematics, Royal College of Science and Technology, Glasgow ; B. B. Parrish, Department of Agriculture and Fisheries for Scotland, Marine Laboratory, Aberdeen ; Prof. P. L. Pauson, Freeland professor of chemistry, Royal College of Science and Technology, Glasgow ; Dr. R. J. T. Pennington, research fellow to the Neurological Unit, Medical School, King's College, Newcastle upon Tyne ; Dr. B. B. Rae, assistant to the Director of Fisheries Research, Scotland, Department of Agriculture and Fisheries for Scotland, Marine Laboratory, Aberdeen ; Prof. J. R. Raeburn, Strathcona-Fordyce professor of agriculture in the University of Aberdeen ; R. M. Sillitto, lecturer in natural philosophy, University of Edinburgh ; Dr. F. Smithies, lecturer in mathematics, University of Cambridge ; Dr. D. W. N. Stibbs, Napier professor of astronomy in the University of St. Andrews, and director of the Observatory ; Dr. A. B. Taylor, Registrar General for Scotland.

Physics at Manchester : Prof. E. B. Paul

Dr. E. B. Paul, who has been appointed to a chair in the Department of Physics of the University of Manchester, was educated at Mallorytown and Brockville Schools and at Queen's University, Kingston, Ontario. From 1942 until 1946 he held an appointment with the National Research Council of Canada at Ottawa and took part in the work on nuclear reactions sponsored by that body in connexion with the development of the Chalk River Laboratories. During 1946–48 Paul studied at Cambridge, where he worked with the 1-MV. high-tension generator of the Cavendish Laboratory and took his Ph.D. degree. He then returned to the Physics Division of the Chalk River Laboratories and undertook an extensive investigation of neutron activation cross-sections which has been widely quoted. Following this, he turned his attention to proton-induced reactions and was for the next few years a leading member of a group which has published many papers on resonant processes in the light nuclei. The high standard of this work both in experimental technique and in theoretical analysis has contributed greatly

to the international reputation of the Chalk River Laboratories. In 1955 Paul was appointed to the Atomic Energy Research Establishment, Harwell, where he is now in charge of nuclear research using electrostatic generators, and is deputy head of the Nuclear Physics Division. Paul is well known for his interest in nuclear structure; he was the first to point out that the collective model could give an excellent account of the properties of levels of light nuclei. His ability in interpretation and his wide experience of high-tension work will be of great service to Manchester, where a vigorous programme of research in low-energy nuclear physics is already in being.

Prof. H. E. Hall

Dr. H. E. Hall, who has also been appointed to a chair of physics at Manchester, is only thirty-two. He was educated at Latymer Upper School and Emmanuel College, Cambridge. He went to the Royal Society Mond Laboratory in 1952 and quickly made his mark as an exceptionally skilled experimenter who was equally at home in the construction of delicate equipment and in the mathematical analysis of his results. He carried out a variety of researches on liquid helium which have led to a significant elucidation of our understanding of its properties. Probably the most important contribution to this understanding was an elegant experiment, in collaboration with Dr. W. F. Vinen, in which they showed that second sound was attenuated when propagated in rotating liquid helium II; this demonstrated very directly the existence of vortex lines. In 1958 he was appointed lecturer in the University of Manchester, and has contributed to the development there of a vigorous low-temperature group; he has also expanded his interests and taken up some interesting problems concerned with the Mössbauer effect.

British Scientific Attaché in Paris: Mr. R. V. Melville

Mr. Richard Melville, of the Department of Scientific and Industrial Research, has been appointed scientific attaché to the British Embassy in Paris. He will advise the British Ambassador on scientific matters and report on French scientific and technical development in the civil field. Mr. Melville, who is forty-seven, will hold the rank of senior principal scientific officer. He has been with the Department of Scientific and Industrial Research since joining the Geological Survey and Museum in 1938. He has recently been on secondment to the International Commission on Zoological Nomenclature as assistant secretary, which has brought him into close contact with French scientists. Mr. Melville, who is French-speaking, has also taken part in scientific expeditions in France and French North Africa. Educated at Wellington College and in the United States, he graduated at the University of Reading in 1936, obtained a special honours degree in geology the following year and obtained his M.Sc. in 1941.

Prof. Peter Pringsheim

Prof. Peter Pringsheim, who will be eighty years of age on March 19, was born in Munich, son of a distinguished mathematician, his mother being formerly an actress. He grew up in a home of culture, music and of literary interest. His sister married Thomas Mann. Prof. Pringsheim spent some time in Cambridge with J. J. Thomson, but then joined Rubens in 1909. His career was profoundly affected by the two World Wars. In 1914 he was attending the British Association meeting in Australia when war was declared and he was interned for its duration. During his enforced leisure he wrote the text of his monograph on fluorescence and phosphorescence which, together with his work in the field of fluorescence of vapours, established him as an authority. Soon after his return from internment he was appointed professor in the University of Berlin, where he remained until dismissed in 1933 because of his partly Jewish descent. He moved to Brussels with his Belgian-born wife; but in 1940 was overtaken by another World War, being arrested and taken to a camp in France. Fortunately, his American friends secured his release and he was able to reach the United States to work first in California and later in the Argonne National Laboratory, although he was not reunited with his wife until 1946. In 1954 he retired to Antwerp but maintained his interest in luminescence.

In the early 'twenties Prof. Pringsheim extended his interest in luminescence to the fluorescence of organic molecules in condensed systems. He contributed to the *Handbuch der Physik* in his field. The years of the Second World War led to a revision of his book, and in 1946 a new, monumental text was ready, perhaps the last possible attempt anyone could make to provide a comprehensive review of luminescence in the gaseous, liquid and solid states. Although he regretted that so much of the war-time advances in luminescence was released after the publication of his book, Pringsheim's text still stands as a landmark in luminescence, with its bibliography only a little short of two thousand references. He completed his own research interests by a post-war incursion into the problems of luminescence and colour centres in the alkali halides, reviving a previous interest in the fluorescence of heavy metal ions complexes in solution. He is one of the few people who has attended almost all the major conferences in his subject and it was a pleasure to see him, even in retirement, participating in the Paris Conference of 1956.

Effects of Radioactivity in the Sea

Research on the effects of radioactivity in the sea is to be undertaken by the International Atomic Energy Agency under an agreement recently concluded between the Agency, the Government of Monaco and the Oceanographic Institute in Monaco. The research, which will be conducted at the Scientific Centre of the Government of Monaco, is related to the problem of possible pollution of the sea through the deposition of radioactive materials. It is aimed at studying: (*a*) the movement of water and marine organisms and the deposition of organic and inorganic matter; (*b*) the distribution in marine organisms of radioactive materials already existing or that may be introduced into various locations; (*c*) the effects on marine life of radioactive materials at various concentration-levels. The programme has been approved by the Agency's Scientific Advisory Committee, which is composed of seven leading scientists from different countries. The research, which will start soon, is planned to extend for three years. The laboratory and working facilities of the Scientific Centre in the Oceanographic Museum and a wide variety of electronic and monitoring equipment will be made available by Monaco. The Oceanographic Institute will put at the disposal of

the project a number of valuable facilities, including marine biology laboratories, oceanographic vessels and some specialized fishing equipment. Certain other facilities, including the 360-ton oceanographic ship *Calypso*, may also be available through the Institute. The Monaco Government will contribute 200,000 French new francs for each year of the research project. The Agency will appoint a chief scientist to be in charge of the research and provide other personnel as well as specialized equipment and technical supplies. Agency fellowships will be awarded for training in connexion with the research project.

Co-operative Nuclear Research

In a written answer to a question in the House of Commons on March 7 as to the projects in which the United Kingdom is participating under the auspices of the European Nuclear Energy Agency, Mr. D. Freeth, the Parliamentary Secretary for Science, named the *Dragon* project at Winfrith Heath for the development of the high-temperature gas-cooled reactor and the Halden project in Norway for the development of a boiling-water reactor. The United Kingdom is also co-operating fully in the general work of the Agency through membership of specialist panels, committees and symposia. The *Dragon* project is managed by an international board, the United Kingdom representatives on which are appointed by the Atomic Energy Authority. According to the report for the year ended March 31, 1960, a start has been made on the construction of the experimental reactor, and Mr. Freeth understood that satisfactory progress is continuing. In reply to other questions, Mr. Freeth said that between 35 and 40 graduate physicists, drawn from physics departments in four universities, are making regular use of the facilities at the Rutherford Laboratory at the National Institute for Research in Nuclear Science, Harwell, and teams from two more physics departments would shortly be doing so. Present estimates indicate that the annual output of qualified scientists and technologists in Britain should reach 20,000 by about 1964, or after only eight years, instead of the 10–15 years recommended by the Scientific Man-power Committee of the Advisory Council on Scientific Policy.

Toxic Chemicals and Wild Life

In reply to a question in the House of Lords on March 9, the Joint Parliamentary Secretary to the Ministry of Agriculture, Fisheries and Food, Earl Waldegrave, said the attention of the Government had been directed to the report issued on February 22 by the joint committee of the British Trust for Ornithology and the Royal Society for the Protection of Birds on the effect upon birds and mammals of toxic chemicals used in agriculture. Comprehensive measures for dealing with this problem were agreed at a meeting last December convened by the Department, at which representatives of these two bodies were present, as well as delegates from the Council of Nature, the National Farmers' Union and the Association of British Manufacturers of Agricultural Chemicals. The measures agreed included a survey by the Ministry's pests officers of reported cases of unusual deaths among birds, foxes and badgers, and the results of the survey are to be reviewed with the interested organizations after this spring. The need for further research into the effects of the use of toxic chemicals in agriculture is being examined by a research study group appointed last year. While the Minister thought that these new arrangements would provide valuable evidence on which to base any further action which may seem necessary, he wished it to be widely known that the Government would welcome full information from naturalists or other interested persons about suspected poisoning of birds or mammals by toxic chemicals.

This reply did not entirely satisfy Viscount Elibank, Lord Hurcomb, Lord Shackleton and others, and points were pressed about the omission of any reference to possible dangers to wild life from the Ministry's 1961 list of approved chemicals, the desirability of independent inquiry and the effectiveness of co-ordination between the Ministry, the Agricultural Research Council and the Nature Conservancy. Lord Waldegrave said that he understood that an appendix to the notification scheme dealing with wild life is under discussion with the Nature Conservancy and other bodies, and he undertook to consider embodying a statement in the list itself in due course. Some concern was expressed as to whether sufficient research is proceeding, and Lord Hailsham, Minister for Science, agreed that co-operation could be improved and promised to consider issuing a statement as to the extent of research in progress. He did not, however, enter on the question of relations or co-ordination between the Agricultural Research Council and the Nature Conservancy, on which he was challenged by Lord Shackleton.

National Research Development Corporation of India

The sixth annual report and statement of accounts of the National Research Development Corporation of India covers the year ended March 31, 1960, in which fifty inventions were reported for development by eleven research institutions and individuals, bringing the total to 553, of which 397 are effectively in hand (Pp. 25. New Delhi: National Research Development Corporation of India, 1960). Thirty licences were negotiated and five processes went into production, making the total licensed and in production 37, with 51 licensed, but not yet in production. A new project on lightning arrestors has been sanctioned at the Indian Institute of Science, Bangalore, at an estimated cost of Rs. 1.60 lakhs. Installation of the pilot plant for phthalic anhydride at the Central Fuel Research Institute, Jealgora, is in hand and that for the de-ionization of cane juice at the National Sugar Institute, Kampur, has been installed. Pilot plant for white cement from felspar and a semi-commercial fluidized bed unit for textiles processing are being created.

New West Durham Borehole

At a recent meeting of the Geological Society at Burlington House, Piccadilly, Prof. K. C. Dunham, of the University of Durham, announced the results of a borehole that is being made at Rookhope in West Durham, and financed by the Department of Scientific and Industrial Research. Prof. Dunham, who has carried out extensive work on the metalliferous deposits of the Pennines, has for many years held the view that these continue to greater depths than have so far been exploited, and that they are related to an underlying granite mass. Support for the latter view has come from measurements of the

variations in the gravity field by Dr. M. H. P. Bott, also at Durham. The borehole has now penetrated the 'hidden' granite 1,280 ft. below the surface, and has thus indicated that valuable minerals continue to three times the depth of local mining. The source of the minerals, nevertheless, lies at still greater depth, and the borehole is being continued.

Journal of Theoretical Biology

THE first question one asks about this, as indeed about any, new journal is why is it necessary? As the chief editor says in his preface, "it has frequently been difficult for an author to find an acceptable medium for theoretical papers" as contrasted with experimental ones; and in this one must regretfully concur. Nevertheless, a journal devoted to theoretical papers over the whole of biology must, one would have thought, have had a unifying objective beyond that of providing an asylum for homeless brain-children. There is excitement abroad in biology to-day, just as there is excitement in cosmology, in nuclear physics, in theoretical chemistry; and it is this excitement which, one feels, a journal of theoretical biology should catch, encourage and sustain. In the first issue there are several mathematical and physical papers which would leave the general biologist rather cold, a philosophical paper and an ecological paper which have little in them to excite the mathematician. There are, however, several papers of the kind one has in mind, dealing with the organization of cellular processes, one of which, by Dr. A. Szent-Györgyi, as might be expected from this author, being especially thought-provoking (*Journal of Theoretical Biology*, **1**, No. 1. Subscription rates: (*A*) institutional subscribers, 12*l*. 6*d*. or 17 dollars; (*B*) subscribers certifying that issues will be for personal use only, 8*l*. or 12 dollars. London and New York: Academic Press, Inc., 1961).

Kybernetik

WE had occasion recently to take note of a new Russian journal which is being translated into English in Britain, concerned with cybernetics (*Nature*, **189**, 795; 1961); our attention has now been directed to another journal, of similar scope, published in Germany, but edited by an international board. This is *Kybernetik*, published by Springer-Verlag of Berlin, and which is edited by a small group of people prominent in the field from Germany, Britain, the United States, Austria, France and the Netherlands. As with the Russian journal, the subject-matter in this relates to the transmission and processing of information and to automatic control processes, both as regards theoretical development within engineering and applications to models of biological functions. *Kybernetik* aims at cultivating experimental and theoretical work within the fields of information theory, control and automata theory, sensory processes and physiology of the nervous system as regards its information handling properties, and the like. The first issue of this journal appeared in January 1961.

New Pulsed X-ray Generator

THE Zenith Radio Corporation announces the production of an X-ray generator which, it is claimed, produces 1-μsec. pulses of high-intensity radiation, with a repetition-rate of up to 30 per sec. The maximum operating voltage is 150 kV., with a current pulse of 130 amp., and a pulse power of about 20 MW. The radiation beam and the resultant radiographs are observed on a fluorescent screen and an image intensifier, which may be used for cine-radiography. The main use of the apparatus would appear to be in the field of industrial radiography under dynamic conditions. It can be used to study the internal structure of sealed vibrating systems which are not observable optically. In one demonstration the structure of a bullet in flight at 4,000 ft. per sec. was observed on a closed-circuit television system. Possible uses in crystal diffraction work under transient dynamic conditions are suggested. The claims for possible medical uses seem to be on less firm ground. It is suggested that the very short pulses can give maximum radiographic information with minimum exposure of the patient. This appears to be based on a misconception that information depends on high-radiation intensity only, regardless of the total energy reaching the X-ray film. In one case, sufficient technical information is given for it to be approximately checked, and this raises doubts. It is claimed that adequate density on conventional film is obtained from a single pulse through 1·5 in. aluminium at 6 ft. Simple calculations from the figures given in the report show that such a procedure would involve a conventional radiographic exposure of 0·13 m.amp. and a radiation dose to the film of a fraction of a milliroentgen. Unless there are undisclosed factors, it is very difficult to imagine the production of adequate radiographs under these conditions. In spite of these questions, this new machine offers hopes of important advances in industrial radiography, probably mainly in the field of precision engineering.

Geology of Ben Nevis and Glen Coe

SINCE the first edition of the *Geological Survey Memoir* on "The Geology of Ben Nevis and Glen Coe" (Scotland: sheet 53) was published in 1916, the district has become somewhat of a national playground, much visited by tourists, mountaineers and parties of geological students. In the second edition (pp. 307, pl. xiii; H.M. Stationery Office, 1960; 35*s*.), Sir Edward Bailey has rewritten and modernized his original publication, to provide a comprehensive account of the classical geological features of this fascinating area. Here one finds, associated with the famous cauldron subsidences, the most spectacular display of plutonic, hypabyssal and volcanic rocks of Lower Old Red Sandstone age known anywhere in Europe; and the neighbouring Highland schists, with their recumbent folds and anticlines, have given rise to more disputes about structure and succession than any other group of British rocks studied in the past half-century. Although much of the memoir is difficult reading because of its content of local detail, the work will be warmly welcomed by the many geologists who frequent this instructive and scenic corner of Scotland.

Calendar of AGARD Meetings

THE Advisory Group for Aeronautical Research and Development (AGARD) of the North Atlantic Treaty Organization announces the following schedule of meetings during April–August 1961: Aero Space Medical Panel spring meeting (Lisbon, April 10–14); Flight Mechanics and Fluid Dynamics Panels, "Stability and Control" (Brussels, April 10–15); Flight Mechanics Panel, "*VTOL/STOL* Aircraft" (Paris, April 17–19); Ionospheric Research Com-

mittee, "Disturbances of Solar Origin on Communications" (Naples, May 15–20); Structures and Materials Panel Symposium on the Material Sciences (Paris, May 15–20); Fluid Dynamics Panel (The Hague, July 17–21); Avionics Panel Technical Meeting, "Microminiaturization" (Oslo, July 24–26); Structures and Materials Panel Specialists' Meeting of the Material Group (Oslo, July 24–26); Eleventh AGARD General Assembly, "Scientific Goals of Space Exploration and Research" (Oslo, July 27–28); Avionics Panel Technical Meeting, "Low Noise Electronics" (Oslo, July 31–August 2).

Methods of Teaching Undergraduates

THE University Grants Committee has appointed the following committee to make a comparative study of undergraduate teaching methods and practices current in the universities and colleges of Great Britain in the fields of arts and pure and applied science: Sir Edward Hale (*chairman*); Prof. R. G. D. Allen, professor of statistics, London School of Economics and Political Science; Dr. D. G. Christopherson, warden, Durham Colleges; Mr. J. S. Fulton, principal, University College of Sussex; Dr. J. H. E. Griffiths, lecturer in physics, University of Oxford; Prof. J. E. Harris, professor of zoology, University of Bristol; Prof. A. G. Lehmann, professor of French, University of Reading; Prof. M. McKisack, professor of history, Westfield College, University of London; Miss M. R. Price, headmistress, Milham Ford School, Oxford; Prof. E. M. Wright, professor of mathematics, University of Aberdeen; Mr. J. S. Morrison, lecturer in classics, University of Cambridge; and Mr. A. Tattersall, University of London (*secretary*).

Announcements

PROF. W. H. MCCREA, professor of mathematics in the University of London (Royal Holloway College), has been elected president of the Royal Astronomical Society, in succession to Prof. R. O. Redman.

LORD HURCOMB, chairman of the Nature Conservancy's Committee for England and a member of its Scientific Policy and Finance Committees, has been appointed chairman of the Nature Conservancy in succession to Mr. Arthur Bryce Duncan, who is retiring from the Conservancy after a long and distinguished period of service.

PROF. A. C. FRAZER, professor of medical biochemistry and pharmacology in the University of Birmingham, has been appointed a member of the Agricultural Research Council, in succession to Prof. K. Mather, who has retired.

PROF. RITCHIE CALDER, professor of international relations in the University of Edinburgh, has been awarded the Kalinga Prize by Unesco for his work for the popularization of science.

MR. R. G. MENZIES, Prime Minister of Australia, is to open a new worsted processing block at the Department of Scientific and Industrial Research's Wool Industries Research Association, Torridon, Leeds, on March 22. Further information can be obtained from Norman Manners, Chief Press Officer, Charles House, 5–11 Regent Street, London, S.W.1.

DR. NORMAN DENNIS NEWELL has been awarded the Mary Clark Thompson Medal of the National Academy of Sciences, in recognition of his outstanding contributions in the field of palæontology and geology, particularly concerning the ecology of modern and ancient calcareous reefs.

THE annual conference of the National Union of Teachers is to be held at the Dome, Brighton, during April 1–6. Further information can be obtained from Mr. F. Jarvis, National Union of Teachers, Hamilton House, Mabledon Place, London, W.C.1. The programme includes an address by Mr. H. D. P. Lee, headmaster of Winchester College, on "Sixth Form Studies", and one by Sir Wilfrid Martineau, chairman of the Education Authorities' Panel of the Burnham Committee, on "Thoughts on Higher Education".

THE Royal Photographic Society of Great Britain is organizing a three-day symposium on "Photography on Expeditions" at the Royal Geographical Society, 1 Kensington Gore, London, S.W.7, during April 11–13. Further information can be obtained from Mr. A. G. Tull, Technicolor, Ltd., Bath Road, West Drayton, Middlesex.

THE spring meeting of the British Radio Spectroscopy Group will be held at the University of St. Andrews during April 6–7. The subjects for discussion are: electron spin resonance in free radicals (April 6) and nuclear magnetic resonance, including high resolution (April 7). Further information can be obtained from D. Bijl and F. A. Rushworth, Department of Natural Philosophy, The University, St. Andrews.

THE Società Italiana di Fisica is organizing an Enrico Fermi international school of physics at Varenna. Five courses are being held as follows: May 23–June 3, cosmic rays, solar particles and space research; June 19–July 1, evidence for gravitational theories; July 3–15, liquid helium; July 17–August 5, semiconductors; August 7–26, nuclear physics. Further information can be obtained from Prof. G. Polvani, Società Italiana di Fisica, Via Saldini, 50 Milano.

THE Institution of Chemical Engineers is holding a one-day symposium in the Chemical Engineering Department, University of Birmingham, on April 12. Among the subjects to be considered are: "Fabrication and Properties of Some of the Newer Constructional Metals" (Dr. N. P. Inglis); "Recent Developments in Wrought Corrosion Resistant Nickel-Base Alloys" (E. Warde); "Plastics in Chemical Engineering and Building" (S. Slaney); "Glass Fibre Wound Laminates" (Dr. F. F. Jaray); "Recent High Temperature Ceramics" (Dr. A. T. Green). Further information can be obtained from T. R. Bott, Honorary Secretary, Midlands Branch, Institution of Chemical Engineers, Chemical Engineering Department, The University, Edgbaston, Birmingham 15.

THE Road Research Laboratory of the Department of Scientific and Industrial Research is holding open days on May 3–4. The work of the Materials and Construction Division and of the Tropical Section will be on show at Harmondsworth, Middlesex, while the work of the Laboratory's Traffic and Safety Division will be on show at the new Road Research Track at Crowthorne, Berkshire. The Scottish Branch of the Laboratory at Thorntonhall, near Glasgow, will be open to visitors during June 7–8. Further information can be obtained from the Press Office, Department of Scientific and Industrial Research, 5–11 Regent Street, London, S.W.1.

THE NUFFIELD FOUNDATION

THE fifteenth annual report of the Nuffield Foundation, covering the year ended March 31, 1960, shows that the disposable income of the Foundation increased by £475,000 to £1,850,000. It welcomes the Charities Act of 1960 as making it easier, speedier and cheaper for a foundation to effect changes in its objects to suit modern needs, and emphasizes the importance of such freedom for the newer type of foundation, in an ever-changing social situation, concerned more especially with the future*. The modern foundation, it is emphasized, is profoundly influenced by the Rockefeller tradition of insistence on search for excellence and its belief that a foundation should evoke from a community a recognition of the need for a particular work the foundation has pioneered, followed by willingness to meet that need out of communal resources.

Of the allocation of £77,260 for science, a further £1,800 was for the work on natural selection and adaptation under Dr. E. B. Ford in the Department of Zoology and Comparative Anatomy, University of Oxford, where Dr. H. B. D. Kettlewell is working on the spread of black moths in manufacturing districts; their invasion of the surrounding country has shown that resting moths are selectively eliminated by birds and has confirmed that industrial melanism is associated with a physiological superiority of the black moths. A further £4,080 over three years went to the Department of Zoology, University of Liverpool, for work on polymorphism in butterflies and the relation between human blood groups and disease, while £1,000 a year for five years was provided for the Biophysical Research Group then under Prof. A. L. Hodgkin in the Physiological Laboratory, University of Cambridge, for its work on the conduction of impulses in nerve and muscle, active transport or secretion of ions through membranes, and on muscular contractions. A grant of £5,700 over three years, covering the salaries of a senior research fellow and a graduate assistant, and the cost of materials, was made to the University of Liverpool for expansion of the work on the organic chemistry of porphyrins under Prof. E. W. Kenner; an extended grant of up to £2,950 to the University College of Swansea is to enable Prof. H. E. Street to examine further the culturability of the excised roots of monocotyledonous species, and to undertake a biochemical study of the influence of light on the growth of wheat roots. Of grants totalling £20,000 in technology, £13,500 over five years to Loughborough College of Technology was to integrate the teaching staff with industry, with a further £500 for a study visit to the United States to make a critical analysis of the relation between academic education in colleges and practical training in industry of professional engineers.

Generally, the tendency during the year was towards larger grants, and grants totalling almost £310,000 in medicine included £62,500 over five years for a Nuffield Unit of Clinical Physiology, at the Postgraduate Medical School, Hammersmith Hospital, University of London; £100,000 to the Zoological Society of London, to found the Nuffield Institute of Comparative Medicine, and create two senior research fellowships; £60,000 (with a subsequent further £100,000) for a Nuffield Hearing and Speech Centre at the Royal National Throat, Nose and Ear Hospital; £25,000 over five years to the United Oxford Hospitals for neurological research, including the development of new techniques, the building and maintenance of electro-physiological equipment, and work on the behaviour and structure of the nervous system when affected by disease; and £18,000 for an extension to the Star and Garter Home for Disabled Sailors, Soldiers and Airmen, Richmond, Surrey. £5,000 over two years was offered to the Institute of Child Health, University of London, for research on biochemical abnormalities and mental retardation, and £6,000 over two years to Guy's Hospital Medical School for investigations into the biochemical basis of temporary psychoses.

In social research and experiment, for which grants totalling £432,000 were made, the Foundation's most important concern was the establishment of a national institute for social work, in accordance with the recommendation of the Younghusband Report, and for this purpose £250,000 was provided. A development fund of £50,000, available at the rate of £10,000 a year, was provided for the Institute of Race Relations, and £11,000 over three years for the School of Oriental and African Studies, University of London, for the first phase of a study of African customary law. Of grants totalling £308,000 in education, £50,000 was to Borough Road Teachers' College, Isleworth, for a science block, to be known as the Nuffield Science Building; £130,000 to the University of Southampton for the Nuffield Theatre; and £60,000 to the University of Leeds for the Nuffield Foundation Unit for the History of Ideas, under the direction of Dr. S. Toulmin.

Allocations for the care of the aged and research in ageing, totalling £140,000, included £122,500 to the National Corporation for the Care of Old People, and £7,100 for the Nuffield Gerontological Research Fellowship at the University of Birmingham. From the Oliver Bird Fund, £38,000 over five years was provided to the rheumatism unit at Edinburgh for a second research fellow, a pathologist, and secretarial and technical workers, while the Department of Experimental Pathology, University of Birmingham, received £22,500 over three years in support of studies on plasma proteins aimed at discovering an antiserum specific for rheumatoid factor as a whole, facilitating assay of the factor in human plasma and more precise localization in diseased tissues.

Grants for the Commonwealth overseas totalling £603,000 included £250,000 to the University College of Rhodesia and Nyasaland for a medical school; £10,000 to the Forestry Department, Entebbe, Uganda, for work on the productivity of tropical high forest; £20,000 towards the cost of the Library at Jan Smuts House, where the South African Institute of International Affairs is centred; a further £7,500 to the Gayaza Girls' High School, near Kampala, to enable the diet side of the experiment on farming and balanced diet to be maintained;

* The Nuffield Foundation—Report for the year ended 31 March, 1960. Pp. xlii+144. (London: The Nuffield Foundation, 1960.)

£45,000 for a Nuffield visiting professorship at University College, Ibadan; £20,000 to endow a chair of anæsthetics at the University of Sydney; £40,000 for the recruitment of teachers of English in North Borneo; and £12,000 to establish a Literature Bureau in Sarawak. £25,000 to the Government of Mauritius was for an investigation into food production and marketing, and £4,200 to the University of Otago, Dunedin, and Canterbury Agricultural College for research into the lactation of sheep.

Allocations under the fellowships and scholarships schemes totalled £226,741. These included two new fellowship schemes in medicine, one of which will enable twelve family doctors practising in the United Kingdom to spend six months abroad during the next four years, studying subjects of importance in general practice. The other is for three types of fellowship in podiatrics. No medical fellowships or dental research fellowships were awarded during the year, owing to the absence of candidates of the desired quality, but one medical research fellowship and four fellowships and four scholarships in dentistry were awarded; three travelling fellowships for Civil Servants were awarded. Under the schemes for the Dominions and Colonies, five travelling fellowships in medicine, fifteen in natural science (and one fellowship in engineering from India) and nine in the humanities and social sciences were awarded, but only eight farming awards were made. Two travelling fellowships were awarded to Indian Civil servants. The Foundation's contribution to the Royal Society and Nuffield Foundation Commonwealth Bursaries scheme was renewed at £5,000 a year for a further five years, and twenty-one awards were made.

THE NATIONAL RESEARCH DEVELOPMENT CORPORATION

THE annual report and statement of accounts of the National Research Development Corporation for the year ended June 30, 1960, differs from the usual pattern, information on the position of development projects being mainly placed in an appendix, while the report itself deals at greater length with the Corporation's financial position after its eleven years of life*. The accounts, which are submitted in the form directed by the Board of Trade, with approval of the Treasury, show that annual revenue from exploitation continues to increase, and in spite of the increase in administrative expenses since 1957, the total income of £316,441 almost balanced the total outgoings of £328,961, apart from external development expenditure of £427,316 and interest of £132,096 on Board of Trade advances. The report suggests that the development projects overall, regarded as assets, may in the event provide a greater return than their value written down in the accounts, but in view of the risks involved the Corporation considers it would be unwise to assign to them a higher value at present. It would be easier to present a picture of the success of the Corporation's development activities if development expenditure remained stable for, say, 15 years, but in fact it has increased substantially from £112,988 in 1954–55 to £427,316 in 1959–60, plus forward commitments amounting to £739,000, and the balance sheet thus probably gives an unduly pessimistic picture of the financial position of the Corporation. Future royalty earnings are also expected to be considerably greater than the asset shown, but can only be assessed on a statistical basis from past experience. Meanwhile, interest on the Board of Trade loans continues to grow, and since the Corporation borrows at fixed rates of interest to cover long-term 'risk' ventures at a level of about double its revenue earnings, by the time returns are received on successful projects, the accumulated interest on borrowings to cover both successful and unsuccessful projects will be a formidable sum.

For all these reasons it is still extremely difficult to predict when the Corporation will be able "to secure, in so far as can be done consistently with the fulfilment of their purposes that the return to them from their activities shall be sufficient to meet their outgoings on revenue account". It seems that it may not be possible to recover enough profit from successful ventures to cover both accumulated interest on loans and losses on unsuccessful projects. Meanwhile, in a written answer to a question about the report, the President of the Board of Trade stated in the House of Commons on January 24 that he had asked the Corporation to consider with his Department the possibility of devising some means of ascertaining more readily what the true financial position is, and in particular of assessing the Corporation's ability to commence payment of interest on the monies advanced to it.

In its exploitation activities, the Corporation completed 81 licence agreements in the United Kingdom during the year as against 61 in 1958–59, and 456 such agreements were in force at June 30, 1960. Royalties and other payments under licence and option agreements amounted to £259,000 compared with £182,000 in the previous year, about half these receipts being derived from overseas business. At the end of the year the Corporation held 597 United Kingdom and 1,015 overseas granted patents and 469 United Kingdom and 1,015 overseas patent applications. Of the 1,021 inventions communicated to the Corporation during the year (compared with 681 in 1958–59), 301 were from Government Departments and Research Councils; 44 from Commonwealth official organizations, 137 from universities, 20 from research associations and 8 from charitable organizations. Private firms and individuals in the United Kingdom contributed 478, in the Commonwealth 15, and elsewhere overseas 18. Of the 255 patent rights assigned, 170 were from Government Departments and Research Councils, 70 from universities, and 11 from industrial research associations.

By the end of the year the Corporation was providing financial assistance for 35 development projects covering a very wide technical field, and some of these, such as hovercraft and fuel cell developments, are of a major character and may involve further large capital commitments. Among the new projects for the year are one for the development of electronic automatic equipment for process plant con-

* National Research Development Corporation. Report and Statement of Accounts for the year 1st July, 1959, to 30th June, 1960. Pp. ii+30. (London: H.M. Stationery Office, 1961.) 1s. 6d. net.

trol, Prof. D. Gabor's project for the thermionic generation of electricity, one for the design of an infinitely variable speed gear, and the development of interferon, a substance which has the important property of interfering with the reproduction of normal virus and may be of wide utility against virus diseases. Major revenue earning inventions during the year include cephalosporin C, tri-iodothyronine, the *Emidec* 2400 electronic computer, Prof. Wain's selective weedkillers, the Hutchinson–Scarrott pulse height analyser, hecogenin, the carbon monoxide detector, an insecticidal fumer, and a microdensitometer. The Joint Development Committee, set up with the Department of Scientific and Industrial Research in 1958 to examine development problems of common interest and advise on the way in which particular development contracts should be handled, has considered and advised on some twenty proposals for research and development during the year; it has proved a useful forum for considering matters of interest to both bodies, ensures that overlapping is avoided, and facilitates the investigation by both bodies of gaps in research and development in both fields.

ADVISING THE FARMER

WITHIN the Agricultural Education Association, a new section, the Advisory Methods Section, has recently been formed, and a series of papers were read at a meeting of this section in London on December 8. The general topic was to be a review of investigations in advisory methods: in practice, only one of the three speakers dealt at any length with research which has already been done, though all were concerned to analyse the advisory process with a view to further research.

Mr. T. Moore, of the Ministry of Agriculture in Northern Ireland, was the first speaker. He began by discussing the ways in which advisers could be most useful to farmers, and gave it as his view that 'trouble-shooting' was not of great value, by comparison with the giving of advice on the broader topic of farm management. This point of view is not uncommon among farm advisers, though the idea that the person providing the advice is better fitted to say what topics he should advise on than the person seeking the advice seems to have some unfortunate implications. If for no other reason, the adviser may well have to appear willing to do some 'trouble-shooting' if he wants to get invited on to certain farms, and successful 'trouble-shooting' in such circumstances may serve to win the farmer's confidence.

Using an arbitrary classification of farmers into three categories, Mr. Moore pointed out that advisers themselves can often learn a lot from the best farmers, that there will be a second group who cannot be helped much, leaving a third group consisting mainly of hard-working farmers who farm mainly by traditional methods. Farmers in this last group are those to whom advisers can be of most use. He claimed, too, that the size of his farm is not a satisfactory indication of how receptive a farmer will be to advice, though he gave no statistical data to support his claim. Without such evidence, the claim seems an unlikely one, for nearly all studies of farmers have shown that acreage is by far the most useful criterion for assessing the progressiveness of a farmer.

Commenting on advisory methods, Mr. Moore quoted some Australian data which stated that farmers visit other farms a good deal, and he thought this emphasized the importance the farmer attaches to seeing a technique in operation. Another interpretation of the same data would be that farmers feel that they can obtain an unbiased point of view in discussion with a practising farmer. Mr. Moore also commented on individual advisory visits to farms, and remarked that some people were somewhat sceptical about their value. He felt that pilot farms were useful, particularly where the farm chosen is not very different in size from other farms in the district, and claimed it as essential that the pilot farmer farms at a profit, regardless of the appearance of the farm. There seems to be some degree of conflict here with theories of leadership, since farmers commonly appear to have a favourable opinion of farmers who operate on a larger scale than themselves, though there are also data suggesting that the difference in scale must not be too great.

Mr. A. W. van den Ban talked about research on advisory methods in the Netherlands, where there are now five rural sociologists engaged in such work, two of them doing this as a full-time occupation. This certainly compares favourably with Great Britain, in which there is not even one such person who is employed to do full-time research in rural sociology. Mr. van den Ban discussed the part that different sources of information play in the adoption process, with the mass media coming in at the early stages, followed by 'individual' sources, such as talking with advisers, or with other farmers. He recommended that the adviser should manipulate the sources of information at his disposal so as to ensure that the farmer receives information in this way: in practice, because the mass media normally reach a farmer before the 'individual' sources, this does not seem to be any guarantee that this is the ideal way.

Dutch farmers were, until fairly recent times, on a subsistence economy and this still affects their way of thinking. When a whole group of farmers feel this way, it is made even more difficult for an individual to be progressive, and even such activities as reading a book or visiting a meeting in the daytime may be frowned on by the community.

Mr. van den Ban discussed the various sources of information, including the mass media, which a farmer can readily ignore since advice cannot be adjusted to individual needs, as well as farm visits, usually made by an adviser who lives among the farmers he serves, and who does not have so much more training than the farmers: this may mean that there is no great difference in status between the local adviser and the farmers, a fact which should make communication easier. Psychologists have been giving training courses to advisers, in an attempt to help them to cope with problems of inter-personal relationships, for example the somewhat delicate situation which may develop

when a young adviser has to tell an experienced farmer, older than himself, how to correct his mistakes.

In the Netherlands, it has been found that most of the progressive farmers have visits from advisers, whereas the traditional ones are less likely to be visited. This is not necessarily bad, as Mr. van den Ban explained, since the traditional farmers may learn from studying what the progressive farmers do. When discussing this, and the more deliberate attempts to promote this type of diffusion process, using pilot farms, Mr. van den Ban pointed out that this mechanism may not operate if the farmer chosen is regarded by others as one who is so skilful, or has such good land, that he is in a different category from themselves. If this occurs, this farmer's example may be ignored because it is felt to be irrelevant to their type of farming.

Mr. van den Ban discussed how farmers who are friends appear to influence each other so that, for example, they are very likely to have the same brand of milking machine. He quoted data to show that farmers felt that attending group discussions had a greater influence on them than attending lectures, and cited data from the United States which appeared to point to the same conclusion. He seemed not to be aware that this American finding has been to some extent discredited by more recent research. Mr. van den Ban concluded by emphasizing the need for directing advisory methods to changing the aims of the community, rather than the aims of individuals, so as not to set the individual in conflict with the community norms.

Mr. H. Burr, of the National Agricultural Advisory Service, gave the last paper. Mentioning the frequently occurring finding that farmers are much influenced by other farmers, Mr. Burr wondered if this could be an artefact due to farmers feeling least damage to their self-esteem by admitting to influences of this kind. This is a fair criticism since these research claims are based on farmers' own reports of what influenced them, though there has been some research recently which shows that farmers will go to a lot of trouble to visit farms where a new technique is being tried, before trying it themselves. With the technique concerned, it seemed likely that a talk with the farmer concerned was being sought, rather than an attempt to learn by seeing the technique in action.

Mr. Burr noted that the National Agricultural Advisory Service as a body strongly favoured the individual advisory visit, but said that some within the Service were trying to 'personalize' group advisory methods, so as to achieve the advantages of both. Mr. Burr also talked about 'leaders', and ways of designating them: self-designation may be misleading and direct-designation, for example, when a pilot farm is chosen by the adviser, has its dangers if the farmer concerned is so different from other farmers that they cannot 'identify' themselves with him. Indirect-designation occurs when farmers are asked to name their leaders, though it is not always easy to be sure that the choice of a farmer whose farm is to be used as a pilot farm, or for a farm walk, does not influence other farmers to regard such a person as a leader. Mr. Burr also pointed out that there are few data to show how much influence such leaders have, nor is it known whether the same farmers are the leaders over a long period. He felt that more should be known about this before the Advisory Service commits itself to using leaders deliberately as an advisory technique.

A lively discussion followed these papers and showed the interest which exists in problems of this type, though, clearly, as the speakers emphasized, much more research is needed. The meeting was, in fact, a most interesting one, and it is to be hoped that this Section of the Agricultural Education Association will sponsor many more. It is heartening to think that a group of people, one of the main tasks of which is to encourage a greater use of scientific advances, should be so concerned to evaluate their own methods of passing on these ideas. D. SHEPPARD

SWISS SOCIETY FOR NATURAL SCIENCES

THE one hundred and fortieth annual session of the Swiss Society for Natural Sciences was held in Canton Aargau during September 23–25, 1960. By a lucky coincidence the main exhibitions connected with the quincentenary of the University of Basle had been extended and were still on view nearby, including the unique Greek treasures and the remarkable display of the University's history, as well as the more purely scientific attraction of the *Oreopithecus* exhibits and the gorilla baby, 'Goma', born in Basle Zoo.

The Aargau meeting opened with a visit to the installations of *Reaktor AG* in a large forest clearing at Würenlingen. Here the first Swiss atomic reactor, *Sapphyr*, originally shown at Geneva, and a second larger reactor are already available for industrial and research purposes in association with Zurich Technical High School. A third reactor, to be larger again, is in process of construction.

The first general assembly was held in the twelfth-century town of Zofingen, cradle of the nation-wide student society Zofingia since 1819, which has been much enlivened by the colourful quinquennial celebrations. Here the central president, Prof. G. Töndury (Zurich), in his address of welcome introduced the opening speech of the annual president, Dr. K. Baeschlin (Aarau), on the main theme of the session, "Der Mensch und seine Beziehungen zur Umwelt". The subject fell into four categories: man and the universe; man and Nature in a geographical sense; man and animal; and man and man. The first two were treated by Prof. M. Waldmeier of Zurich ("Die Beziehung Mensch-Weltall"), and Prof. L. Emberger of Montpellier ("La Relation Homme-Nature") at the first general assembly. The second two, by Prof. O. Koehler of Freiburg in Breisgau ("Die Beziehung Mensch-Tier"), and Prof. W. Löffler of Zurich ("Die Beziehung Mensch-Mensch"), were given at the second general assembly, in the now State-owned Castle of Lenzburg, once (1892–1911) the possession of Lady Mildred Bowes-Lyon and her American husband, Aug. E. Jessup, to whom is due the present good condition of the property, maintained after them (1911–56) by the last private owners, the family of Lincoln Ellsworth, the arctic explorer in partnership with Amundsen.

All four lectures will appear in full in the *Acta* of the Society. Each began with a brief historical survey and underlined lessons to be learnt from the past, but the emphasis was on new knowledge, and some particular aspect was focused in each case. Prof. Koehler illustrated by striking film-sequences the often disregarded capacity of animals to learn, with extreme rapidity, and without direct guidance from man. Prof. Löffler, who had been deliberately chosen as an eminent medical practitioner in preference to a psychiatrist for the subject of human inter-relations, had naturally some words of warning on present-day ethics in his profession, and lent the conviction of intimate experience to the plea for better family relations which both mental and physical welfare specialists endorse to-day, besides surveying the field of modern mass-problems of over-ageing, over-population, hunger and over-production which science must help to solve. Prof. Emberger was inclined to stress the destructive influences of man on Nature more than the work of reclamation by his illustrative slides on this urgent topic of the day. Prof. Waldmeier could not but give much place to modern developments in space-research and the formerly unthinkable extension of experimental techniques to astronomy.

Some of the sectional proceedings were designed to fit into the same general theme of "Man and his Relations to his Environment". A symposium on statistical methods in biology and medicine, organized by the Swiss Society for Medical Biology, in conjunction with the Mathematical Society and the Society for Logic and Philosophy, had for its topics: development and prognosis of the death-rate in Switzerland (P. Nolfi, Zurich); development of the cancer death-rate, with special reference to lung cancer (H. Wiesler, Zurich); medicine and statistics (E. Tanner, Zurich); medicine and logic (E. Batschelet, Basle); optimal information by use of statistical methods (L. Le Roy, Zurich); statistics as an aid to medical research (D. Högger, Zurich).

The medical and psychological scene was prominent also in the historical section, notably in a contribution by Madame A. Virieux of Rolle, "Quelques Remarques à propos de la Psychologie à l'Antiquité", in which she pointed out, among other things, that Plotinus's theory of a two-fold memory—one purely spiritual, one body-linked—influenced Bergson; that the contrast between Socrates, who believed emotion to be entirely governed by reason, and Aristotle, in his recognition of the intimate union of body and soul, is of great relevance to modern psycho-somatic theory. Anxiety as treated by Aeschylus anticipates Freud. The fact that Plato, in his extensive study of vision, took colour to be a subjective phenomenon, in the sense of an original product for each individual of the complex visual process, seems as striking as the subtle and still little-understood fusion he attempted (probably in order to explain the redressing of inverted images) of the two opposing theories of currents emerging from the eye and the object respectively, as the basis of that process.

Psychological and social influences were touched on in a context of recent mathematical history by Dr. R. C. H. Tanner (London) on "W. H. Young et la Méthode des suites monotones", with reference to Young's anticipation by Henri Lebesgue in extending the scope of the Riemann integration process. This discovery was incidental to a much wider field of research for Young, and the setback cannot have made on him the emotional impact assumed by his English biographers, while the role attributed to it in the lack of recognition he received from British appointments boards during his life-time can only, if admitted, impugn the 'cult of results' and lack of methodological insight then common in England; an offshoot perhaps of a competitive and sporting tradition that dies hard.

The mathematical section in its own right made a relatively modest show, because, evidently, of the special effort during June 25–26 in celebrating the Swiss Mathematical Society's half-centenary at Zurich, when the following contributions were made: Prof. M. Plancherel (Zurich) on "Mathematiques et Mathematiciens en Suisse (1850-1950)", Prof. H. Hopf (Zurich) on "Einige neuere Ergebnisse in Differentialgeometrie und Topologie", Prof. G. de Rham (Lausanne) on "Quelques Notions de Base de la Theorie des Variétés Intégrables"—the last two coincided with the international colloquium on "Differential Geometry and Topology", held under the auspices of the International Mathematical Union during June 20–25. At a special ceremony, the topologists Prof. H. Whitney (Princeton), Prof. J. Leray (Paris) and Prof. G. de Rham were honoured and given commemorative scrolls by the annual president of the Swiss Mathematical Society, Prof. H. Jecklin (Zurich).

The physical section concentrated largely on nuclear and allied research; the chemical section also had on its list one paper on the role of heavy metals in the mechanism of radiation damage and shielding (W. Brintziger, Basle), but for the rest it devoted itself mainly to more classical synthetic and reaction chemistry.

The section for geophysics, meteorology and astronomy heard Prof. Jean Lugeon, head of the Swiss Meteorological Station, Zurich, report on radiosonde measurements in connexion with the industrial air-pollution at Aigle, which he has been actively campaigning against in recent years. J. Riecker, of the same Station, spoke of sunrise in the ionosphere and its repercussions on long-wave propagation. G. Barnes, an Australian who is temporarily at the Technical High School, Zurich, discussed the prevention of water evaporation by surface films. There were also reports on the expedition to El Aaiun in the Spanish Sahara for the total eclipse on October 2, 1959 (Prof. M. Waldmeier of the Federal Observatory, Zurich), and on the unusual fluctuations in the ozone content at different heights in the stratosphere during the sudden heating up in January–February 1958 (H. Dütsch, Zurich). Other communications concerned rain and ice, and climatological problems. In the botany section, the items of special local interest were outweighed by the research work of general import of the strong Geneva school, with F. Chodat and others, and two obituary notices: "W. Vischer 1890–1960", a promoter of the Swiss Society for the Protection of Nature, by M. Geiger-Huber (Basle), and "Eduard Rübel 1876–1960", by W. Lüdi (Zurich).

Two recent international congresses were reported by members who had taken part: that on "Logic, Methodology and Philosophy of Science", at Stanford, by E. Walter (Zurich) and I. M. Bochenski (Freiburg), and that on "Geography", at Stockholm, by E. Schwabe (Berne).

R. C. H. Tanner

HEALTH IN INDUSTRY

IN a foreword to a publication issued by the Ministry of Labour, the Minister, Mr. John Hare, directs attention to the fact that more than 300 million working days are lost each year in Great Britain because of sickness or injury.

The Minister's foreword is contained in the booklet, *Health at Work**, which gives fourteen examples of individual industrial health schemes operating successfully in factories in different parts of Great Britain, and the Minister hopes that these examples will encourage other firms to follow suit. The booklet is being widely distributed to factory occupiers by H.M. Factory Inspectorate. It deals with such questions as how factory medical services are organized, and what they achieve, the attitudes of workers to their introduction and the advantages derived by both employer and worker.

In carrying out the survey, the Ministry obtained from each factory details of the nature of the work done there, the organization of the medical services, the work of the medical officers and nursing staff, and the cost of each scheme. Four of the factories employ from 231 to 300 workers; five employ from 500 to 1,000; three from 1,000 to 5,000, and two more than 5,000. Included in the industries represented are heavy engineering and foundry work, copper and metal refining, the manufacturing of electric cookers, refrigerators, electro-plated ware, carbon black, printing machinery, animal feeding stuffs and vegetable oil. Also included are wool and worsted spinning, the processing of asbestos yarns and pipes, and the preparation of insecticides, fungicides, fine chemicals and pharmaceuticals.

Fear about costs is suggested as being the biggest single factor in preventing a more rapid spread of industrial health schemes. The booklet gives detailed figures of the cost of the schemes provided. The annual running costs vary widely according to the nature of the services provided and the numbers employed. Of the 14 schemes described, seven cost £2 or less a head per annum, five cost between £2 and £3, and the other two more than £3. The booklet also mentions an attempt at another factory to weigh in terms of cash the worth or value of such a scheme. This led to the conclusion that, on a conservative estimate, the annual recurring costs of the medical scheme were more than covered by savings in time lost, and that the long-term benefits in better health and morale were a bonus alike to the company and the employee.

It is emphasized that the booklet does not intend to provide a ready-made pattern from which an employer can pick a scheme to suit his pocket, or the size of his factory and his business. What it does show is how, in practice, such schemes are operating to meet particular needs of particular firms, and the considerable variety of functions which the services can perform to the advantage of employers and workpeople. The reasons why firms considered it worth while to spend more money voluntarily on medical supervision varied according to the type of industry, but the following were typical: (1) the pre-employment examination was a safeguard to management and workers; (2) from a practical point of view, speedy attention to accidents and ill-health saved time; (3) improvement in relations between employers and workers resulted from such a scheme.

The general impression drawn from reactions on the part of workers was that schemes of medical supervision described in the booklet provided a personal service which the workers greatly appreciated. The fact that immediate and expert attention could be given to the injured and sick aroused a feeling of confidence among them. The booklet indicates that in one or two instances there was some initial suspicion on the part of workers which soon disappeared with experience of the working of the schemes.

* Ministry of Labour. *Health at Work: a Description of Medical Services in Fourteen British Factories*. Pp. 76. (London: Ministry of Labour, 1960.)

ELM DISEASE

ALTHOUGH the elms are not, nowadays, regarded as important species in forestry proper, the Forestry Commissioners sometimes feel that it is incumbent on them to devote time and money to conduct research into problems concerned with trees in which the British public as a whole are generally interested. A recent publication*, which would have been more correctly described as referring to southern England, deals with such a case. It is concerned with a fungous disease of elms caused by *Ceratostomella ulmi* (Schwartz) Buis., which was first recorded in France in 1918, and in Holland in 1919, and is suspected as having been introduced with elms imported from eastern Asia. It soon became widespread in northern Europe and in North America.

It was first recorded in England in 1927, by which time it was giving much concern to tree-growers in Holland, where its severity at one time earned for it the title of the Dutch elm disease. The effect of the fungus is to cause a vascular wilting of the leaves followed by the death of twigs and branches and even of whole trees. The unsightliness of the dead trees must have attracted the attention of all who travel through those counties where elms are such a notable feature of the landscape. The disease was probably present in Great Britain before its first recording.

The task of studying this disease and of keeping an eye on it was entrusted by the Forestry Commission in 1928 to Mr. T. R. Peace while he was stationed at the Imperial Forestry Institute, Oxford, and he has continued to do this since his appointment to the staff of the Commission, where he is now chief research officer. The present publication, issued by

* Forestry Commission. Bulletin No. 33: The Status and Development of Elm Disease in Britain. By T. R. Peace. Pp. iv + 44 + 76 plates. (London: H.M. Stationery Office, 1960.) 10s. net.

the Forestry Commission, is based on his work, and especially on surveys undertaken by him, during the 31 years up to 1959, but he also acknowledges his debt to American workers in Great Britain in the same field.

This disease is one in which there is a very intimate connexion between two organisms, one from the plant world, the other from the animal world. In 1931 this was established by Fransen, who found that bark beetles of the genus *Scolytus* were carriers of the fungus, which can also enter the tree through wounds and especially through the roots, which, from the suckering habit of the English elm, must be not uncommon.

The surveys revealed that the disease reached its peak in 1931, and that it has steadily declined since 1936–37, not only in the number of elms attacked but also more especially in the severity of the damage caused. It is suggested that the war-time clearance of diseased elms, made possible by the opportunity to market the timber, may have led to a reduction in the beetle population and to infections due to it. It is estimated that the total loss due to the disease lies between 10 and 20 per cent of tree elms, and that this is being made good by sucker growth. Two lines of action were taken to combat the disease. In Holland and the United States a policy of widespread felling of diseased trees was adopted; in Great Britain things were left to run their course. In view of the considerable degree of recovery of diseased trees, in support of which the author provides many good plates, he is perhaps justified in concluding that the loss of elms would have been much greater in Britain if the first policy had been adopted. He advises the awaiting of the field trials of strains resistant to the fungus before widespread planting of elms in hedgerows or for amenity is undertaken. The disease may long continue as a minor nuisance, but is not expected to bring about the disaster of complete annihilation of the elms immemorial. The great weakness of the investigation undertaken by Mr. Peace is one that is associated with most of the publications of the Forestry Commission, namely, lack of appreciation of the importance of allowing for locality differences. The data in respect of both climate and soil are quite inadequate for the treatment of such an exacting genus as *Ulmus*. When a study is allowed to range over a wide variety of site conditions, it is essential that it should be handled in such a way that site variation is allowed for.

M. L. ANDERSON

PHOTO-EMISSION FROM METAL SURFACES MEASURED WITH GEIGER COUNTERS

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DURING the past several years, J. Kramer has investigated a group of phenomena involving the emission of low-energy electrons from solid surfaces. The findings are summarized in two of his papers[1]. This work by Kramer, more recently extended by others, provides an interesting and sensitive new method for investigating the surface condition of both metals and non-metals. Through studies of this so-called Kramer effect, some insight has been gained into a number of phenomena, such as the delayed emission of electrons ('exo-electrons') that occurs when certain non-metals (for example, aluminium oxide powder and gypsum) are crushed or irradiated; the dependence of photo-emission on surface treatment of metals; and electron emission caused by heating below the temperature of thermionic emission. For purposes of theoretical interpretation, and determination of possible practical applications, it is essential to know whether these phenomena are inter-related, and to what extent. The purpose of this article is to report some preliminary experimental observations obtained during an investigation of these phenomena in our Laboratory that we believe are pertinent to this problem.

The emission of low-energy electrons from bulk specimens of several metals of commercial purity (aluminium, tin, copper, nickel and zinc), before and after various mechanical treatments (abrasion, filing, polishing and compression), was measured by means of windowless Geiger-flow counters at room temperature. The specimen, in the form of a disk, ¼ in. thick and 1 in. in diameter, formed a part of the cathode; in one of the counters with a fused quartz envelope, the specimen constituted the largest part of the cathode. The distance of the anode 'point' of the counting tube from the specimen was ⅜ in. The tubes were operated in the voltage-range of 1,200–1,300, where the extent of the plateau was at least 150 V. The flowing gas, at atmospheric pressure, consisted essentially of helium (about 98·5 per cent) and contained *iso*butane as the quenching agent; a small amount (about 0·05 per cent) of water vapour was detected in this gas by mass spectrometry. The background radiation during these measurements was determined to be about 25 counts per minute.

Contrary to the findings of some investigators[2], we detected no emission of electrons from the freshly abraded, filed, or compressively strained metal specimens when the Geiger counters were made completely light tight. In other tests we have made with a quartz-envelope Geiger counter, emission was detected only when the light shielding was not adequate. Evidently, the intensity of stray light needed to induce photo-electron emission from mechanically treated metal surfaces is extremely low. Thus it appears that true delayed emission of low-energy electrons (exo-electrons) does not occur in the absence of any stray light during the detection phase of the experiment.

The blackening of photographic emulsions in contact with freshly deformed or abraded metal surfaces (the so-called Russell effect) is known to result from the formation of hydrogen peroxide at

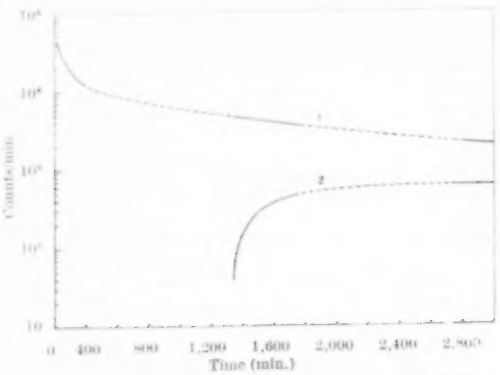

Fig. 1. Photoemission from filed tin surface before and after irradiation. (1) Decay curve of filed tin surface; (2) recovery curve of filed tin after 1-min. irradiation at 50 kV. and 40 m.amp. A tungsten target X-ray tube was used. This sample had reached the decay-level of that in curve 1 at the time of irradiation. Note: Broken lines indicate intervals during which no readings were taken

the metal surface. Grunberg[3] has associated the formation of hydrogen peroxide, in the presence of water vapour and oxygen, with the emission of low-energy exo-electrons. The macroscopic aspects of both the Russell effect and exo-electron emission have been rather thoroughly investigated. Recently, however, Meleka and Barr[4] have applied an autoradiographic technique to a study of the microscopic features of the Russell effect. They found that high-resolution photographic emulsions applied to surfaces of statically strained, high-purity zinc, single-crystal rods were blackened in microscopic areas (lines or rows of dots) corresponding to slip lines associated with varying amounts of slip displacement. In addition, they suggest that exo-electron emission from plastically deformed metals also originates from slip bands on the surface. In view of the fact that we have been unable to detect electron emission from abraded or deformed metal surfaces in complete darkness, it seems to us that the mechanism of the Russell effect cannot be explained by the action of delayed electrons detectable in a Geiger counter.

It is well known that X-ray irradiation of certain non-metals, such as aluminium oxide powder, may induce true delayed electron emission. We have confirmed this observation, and, in addition, have found that the intensity of the delayed electron emission is closely associated with the amount of water contained in the aluminium oxide powder. The emission from samples containing 3 per cent water was about 50 times more intense than that from samples containing about 1·5 per cent water. A similar connexion between electron emission and adsorbed water, during heating and cooling of quinine sulphate, has been reported by Kramer[1].

Our experiments on the X-ray irradiation of metals have demonstrated that such treatment not only does not induce delayed electron emission, but also strongly de-activates the materials with respect to photo-emission. The curves of Fig. 1 show the effect of X-ray irradiation on the photo-emission of a filed tin surface. Other metals have exhibited similar behaviour, with a varying rate of recovery of photo-emission. There is a formal similarity between the 'fatigue' caused by intense light and this de-activation by X-ray irradiation; however, the X-ray fatigue seems to be a more complex phenomenon. Further work is planned to investigate this de-activation by irradiation and the recovery of photo-emission in different atmospheres.

Photo-electric wave-length thresholds were determined by means of the counting arrangement previously described, and a grating monochromator and an incandescent ribbon lamp as a light source. The thresholds were found to be in the near ultra-violet region of the light spectrum, and they differed slightly for the different metals. Table 1 shows the estimated values of these thresholds, together with those reported in the literature for the same pure metals in vacuum.

Table 1. Photoelectric Thresholds

	Filed		X-irradiated		Pure metals in vacuum (ref. 5)	
	Wave-length (Å.)	eV.*	Wave-length (Å.)	eV.*	Wave-length (Å.)	eV.*
Al	4000	3·07	3500	3·51	2950	4·20
Zn	3600	3·41	3300	3·72	2900	4·27
Sn	3500	3·51	3200	3·84	2820	4·39
Cu	3000	4·09	2900	4·24	2770	4·48
Ni	3200	3·84	3000	4·09	2520	4·91

* Electron volts.

These wave-length thresholds follow, in general, the same order as that for pure metals in vacuum, and differ from them by several hundred Ångstrom units. No selective maxima in the visible part of the spectrum were found, which agrees with the observations of Sujak[6].

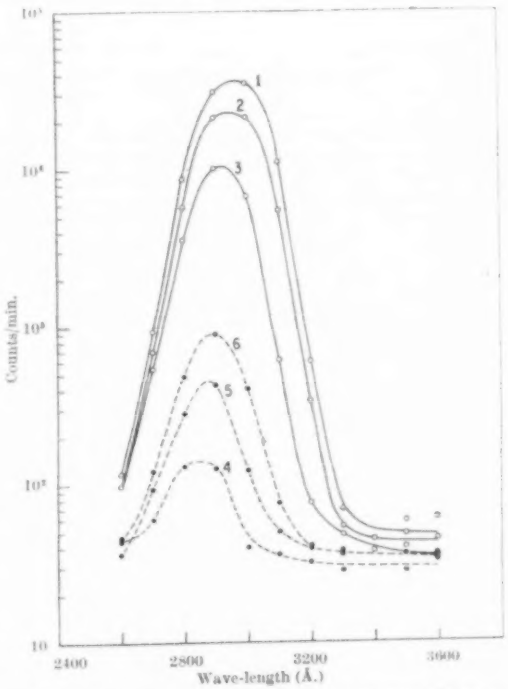

Fig. 2. Decay curves from filed tin, before and after irradiation. (1) Immediately after filing; (2) 50 min. after filing; (3) 1,100 min. after filing; (4) immediately after 1-min. irradiation at 50 kV. and 40 m.amp., tungsten target X-ray tube; (5) 35 min. after irradiation; (6) 400 min. after irradiation
Note: Each point is an average of two readings, symmetrically spaced with respect to the beginning and the end of the run, to minimize the effects of light fatigue

The decay and recovery curves for photo-electric emission from tin, obtained at various intervals after mechanical treatment, are shown in Fig. 2 as a function of wave-length. The maxima in the curves are a result of the combined effects of: (1) a rapid decrease in intensity of the light from the incandescent source with decreasing wave-length, and (2) the rapidly increasing photo-sensitivity with increasing wave-length. These maxima provide a sensitive, qualitative criterion for a shift of photo-sensitivity with change of wave-length. A shift of the maxima of up to 200 Å. was observed in some metals because of differences in surface condition, that is, abraded, irradiated, or after subsequent recovery.

Results such as shown in Fig. 2, as well as other results obtained with a mercury arc light source in the shorter wave-length region of the spectrum, although not yet conclusive, may contribute to an understanding of the increased photo-emission yield resulting from mechanical treatment of metal surfaces. Of particular importance is the question of whether this increase is caused solely by a lowering of the work function of the metal surface. The role of adsorbed gases and oxide films on the metal surface is also of interest.

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ACTIVE SENSITIZATION TO TUBERCULIN WITH CELLS FROM TUBERCULIN-SENSITIZED GUINEA PIGS

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THE cellular transfer of tuberculin hypersensitivity in guinea pigs was first demonstrated by Chase[1]. Transfer with disrupted peripheral blood leucocytes has been demonstrated in man[2] but not in guinea pigs[3]. After passive transfer, to non-sensitized animals, of live cells from guinea pigs hypersensitive to tuberculin, the recipient may show skin hypersensitivity to tuberculin for 3 months or more. This might be explained by survival of the donor cells or by active sensitization of recipients superimposed on the passive hypersensitivity transferred with the donor cells. The following experiments indicate that the second explanation is probably the true one.

Guinea pigs of the Hartley strain were actively sensitized with tubercle bacilli killed by heat and suspended in a Freund's type emulsion[4]. Spleen cells and lymph node cells were prepared as described previously[4]. Peripheral blood leucocytes were prepared by sedimenting the red cells from blood with 6 per cent dextran in saline and centrifuging the supernatant at 230 *g* for 15 min. The remaining contaminating red cells were then lysed in 0·05 *M* sodium chloride for 1 min. Preparations of peripheral leucocytes from individual animals contained 0·5–2·5 × 10^8 cells, while those from spleen and lymph nodes contained between 5 and 10 × 10^8 cells. Cell preparations were disrupted by freezing and thawing seven times in the presence of 0·1 mgm. deoxyribonuclease (Worthington Biochemical Corporation). Complete disruption of the cells was confirmed under the phase contrast microscope.

Live cell preparations were transfused intravenously, and disrupted cell preparations were injected intradermally into multiple sites on to one flank of the guinea pig. All skin tests were with 40 µgm. tuberculin (Mammalian *PPD*, from the Ministry of Agriculture's Veterinary Laboratory, Weybridge), which had been previously dialysed to remove the glycerol. Skin reactions were read 24 hr. after testing. Tests for anaphylaxis were with 2 mgm. *PPD* intravenously. Skin homografts from the donors of live cells were transplanted according to Billingham and Medawar[5].

The results of the transfusion of ~10^9 live cells from the spleen and/or lymph nodes of individual hypersensitive donors are shown in Table 1. The recipients were grafted with skin from the donors of the cells, and received their first skin test immediately after the transfusion. No correlation was observed between retention of skin graft and persistence of tuberculin sensitivity, and it is therefore very unlikely that the donor cells survived beyond one week. The one guinea pig which retained its skin graft for more than one month was found to have lost its tuberculin sensitivity by this time. Seven of the 13 guinea pigs maintained their sensitivity on repeated testing for more than 3 months, and 6 of these showed anaphylaxis when given 2 mgm. *PPD* intravenously at the end of this time.

Guinea pigs which had received intradermal injections of disrupted cells from hypersensitive donors were skin tested with *PPD* 5 or 6 times over a period of nearly 3 months, as shown in Table 2. Weak sensitivity to tuberculin developed 7–14 days later, in animals that had not had any previous injections of *PPD* and strong reactions were found on re-testing after 17 days. Half the animals showed strong reactions >11 × 11 mm. at some

Table 1. PERSISTENCE OF TUBERCULIN HYPERSENSITIVITY AFTER PASSIVE TRANSFER OF APPROXIMATELY 10^9 CELLS INTRAVENOUSLY

Day of skin test	Number of animals showing skin test reaction (40 µgm. *PPD*) after 24 hr.		Proportion rejecting skin graft	Anaphylaxis (2 mgm. *PPD* intravenous)
	Greater than 10 × 10 mm.	7 × 7–10 × 10 mm.		
0	6	7		
9 days	5	5	10/13	
1 month	4	2	12/13	
2 months	7	—		
3 months	7	—		6 (3 died, 3 mild)

Each of 13 guinea pigs received cells from one donor only and was grafted with skin from this animal.

Table 2. Development of Active Sensitization to Tuberculin in Guinea Pigs receiving Disrupted Cells from Peripheral Blood, Spleen, and Lymph Nodes of Hypersensitive Donors

		Days after injection of cells						
		0	7	13–14	17–25	33–43	61–65	82–85
	Peripheral leucocytes (~1 × 10^8 cells)							
	No. tested	3	6	8	5	11	8	8
(a)	Strong reactions*	0	0	0	2	4	4	3
	Weak reactions	0	1	4	1	4	1	1
	Anaphylaxis†							7 (3 died)
	Spleen (~5 × 10^8 cells)							
	No. tested	3	6	9	6	12	9	9
(b)	Strong reactions	0	0	0	0	0	2	4
	Weak reactions	0	1	4	3	7	1	3
	Anaphylaxis							8 (6 died)
	Lymph node cells (~5 × 10^8 cells)							
	No. tested			6	3	6	3	3
(c)	Strong reactions	—	—	0	1	1	1	1
	Weak reactions			4	0	2	0	1
	Anaphylaxis							2 (1 died)
	No cells							
	No. tested	9	9	—	9	—	9	9
(d)	Strong reactions	0	0	—	0	—	0	0
	Weak reactions	0	1	—	0	—	0	2
	Anaphylaxis							2 (none died)

* Strong reactions were >10 × 10 mm.; weak reactions 7 × 7 to 10 × 10 mm. † Tested with 2 mgm. *PPD* intravenous.

stage or other and only 2 out of the 18 animals, which were followed over the whole period, failed to show any reaction. As a control, 9 normal animals were skin tested with *PPD* 5 times over a similar period. One of these showed reactivity on the second injection 7 days after the first, and afterwards failed to react, and 2 others showed very mild reactions which appeared only at the end of the three months course. When frozen and thawed peripheral blood leucocytes and spleen cells from normal unsensitized animals were used the recipients behaved like the control group with no cells.

At the end of the experiment all four groups were challenged with 2 mgm. *PPD* intravenously. Sixteen out of 18 animals which had received disrupted cells from hypersensitive donors developed anaphylaxis and 10 died. Only 2 of the 9 controls developed very mild anaphylaxis.

From these results it appears that a transient delayed hypersensitivity is transferred by intact peripheral blood leucocytes, spleen cells and lymph node cells, and that it may be followed by a superimposed active immunization which persists far beyond the time when the donor cells would have been destroyed by a homograft reaction. Peripheral blood leucocytes were more effective in respect of active sensitization than cells from the spleen and lymph nodes. A further property of cells from sensitized donors is that they can enhance the development of antibody against tuberculin accompanying multiple injections of *PPD*. *PPD* is not a single substance, and there is no evidence whether the antibody is directed against traces of contaminating antigen which are known to be present.

These experiments indicate that the possibility that active immunization has occurred must be borne in mind in the interpretation of experiments on passive transfer of delayed hypersensitivity.

I would like to thank Dr. J. H. Humphrey for his advice throughout this investigation.

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ENZYMATIC SYNTHESIS OF POLY-β-HYDROXYBUTYRIC ACID IN BACTERIA

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THE polymeric ester, poly-β-hydroxybutyric acid, originally discovered by Lemoigne in 1927 as a major component of *Bacillus megaterium*, has since been found to be an important storage material in a variety of bacteria[1–4]. It serves as an intracellular reserve of carbon and reducing power in the photosynthetic bacterium, *Rhodospirillum rubrum*, and as the principal substrate for the endogenous respiration of certain aerobes[3–5].

The present report deals with the synthesis of the polymer from carbon-14-labelled D(−)-β-hydroxybutyryl-coenzyme *A* by particulate fractions of cell-free extracts from *B. megaterium* and *R. rubrum*.

Radioactive D(−)-β-hydroxybutyric acid was obtained by alkaline hydrolysis of purified polymer isolated from cells of *R. rubrum* that had assimilated uniformly labelled acetate in the light[3]. The acid was purified by paper chromatography, and the coenzyme *A* derivative was prepared by the mixed anhydride method of Wieland and Rueff[6]. Free β-hydroxybutyric acid was removed from the acidified solution by ether extraction. Analysis of the specific

Table 1. SYNTHESIS OF POLYMER BY *B. megaterium* EXTRACTS

Time (min.)	Percentage carbon-14 recovered in polymer fraction		
	Exp. 1	Exp. 2	Exp. 3
0	0	0	0
5	—	27	—
10	—	35	—
20	33	45	46
40	36	44	—

The reaction mixtures contained either recombined particulate and supernatant fractions (1·08 mgm. polymer and 1·75 mgm. protein per ml.) or resuspended particulate fraction alone (1·08 mgm. polymer and 0·13 mgm. protein per ml.); and the following components (in μmoles per ml.): magnesium chloride, 12·5; glutathione, 12·5; and potassium phosphate buffer, *p*H 7·4, 125.

Exp. 1: particulate + supernatant fractions + 0·48 μequiv. DL-(−)-β-hydroxybutyryl-coenzyme *A* per ml. (initial); Exps. 2 and 3: particulate fraction + 0·24 and 0·48 μequiv. D(−)-β-hydroxybutyryl-coenzyme *A* per ml. (initial), respectively.

The reaction mixtures were incubated at 33° C.

activity of the product, coupled with hydroxamate and sulphydryl determinations, indicated that at least 95 per cent of the acid was present in thioester combination. Since the commercially available coenzyme *A* used for the synthesis is only 50–75 per cent pure and is contaminated with other sulphydryl compounds (for example, glutathione), the assays reflect the total concentration of β-hydroxybutyryl thioesters, rather than of the coenzyme *A* derivative alone. Poly-β-hydroxybutyric acid was assayed with a modified hydroxamate method for ester determination[7], or by the spectrophotometric method of Slepecky and Law[8].

B. megaterium, strain Km, was grown in the medium containing 2 per cent glucose described by Macrae and Wilkinson[4]. The cells were gathered at the end of exponential growth and washed with 0·033 *M* phosphate buffer, *p*H 7·0. Cell-free extracts were prepared by the osmotic lysis of concentrated protoplasts made by lysozyme treatment of the cells[9]. The lysates were subjected to sonic oscillation to liberate the polymer particles from the cell membranes. The heavy particulate fraction (consisting mainly of polymer particles) was separated from the extract by centrifugation at 3,000 *g* for 20 min. at 4° C., and the particles were washed several times with phosphate buffer, *p*H 7·0. The supernatant fraction contained both the soluble proteins of the cell and the disintegrated cell membranes.

The particulate fraction was incubated with radioactive β-hydroxybutyryl-coenzyme *A* in the presence and absence of the supernatant fraction. The reaction was stopped by addition of alcohol (60 per cent final concentration) and the radioactivity of the isolated polymer was measured. The particles were sedimented by centrifugation, treated with alkaline hypochlorite, washed successively with water and acetone and finally dissolved in chloroform[3,4]. Suitable aliquots were analysed for radioactivity. Controls were performed with reaction mixtures in which β-hydroxybutyryl-coenzyme *A* was replaced by labelled β-hydroxybutyrate in the presence or absence of coenzyme *A*, as well as by alkali-hydrolysed coenzyme *A* derivative. No incorporation of radioactivity into polymer was observed in the control reaction mixtures. In the presence of β-hydroxybutyryl-coenzyme *A*, on the other hand, the polymer became rapidly labelled with carbon-14 when the particulate fraction was used either alone or in combination with the supernatant fraction (Table 1).

The reaction came to completion in about 20 min., at which time 35–45 per cent of the total radioactivity was recovered in the polymer. The observed maximal conversion of thioester to polymer does not give any information on the equilibrium constant for the synthesis of polymer from β-hydroxybutyryl-coenzyme *A*, since the true concentration of the latter compound was not known for reasons previously discussed.

To study the stoichiometry of the reaction, a further experiment was performed in which the disappearance of thioester was measured. The analyses showed that in a reaction mixture initially containing 1·2 mgm. washed polymer particles (without supernatant fraction) and 1·2 μequiv. of thioester per ml., 0·5 μequiv. of β-hydroxybutyrate was incorporated in the polymer, while 0·6 μequiv. of thioester had disappeared. Thus, the synthesis of polymer accounted for more than 80 per cent of the thioester decomposed.

To identify the product unequivocally, the labelled polymer from the above experiment was diluted with purified carrier polymer[3,4] and reprecipitated three times from chloroform: twice with 95 per cent ethanol and once with acetone–ether (2 : 1). The specific activity remained constant throughout. The reprecipitated polymer was hydrolysed for 22 hr. at 30° in *N* potassium hydroxide, treated with cation exchange resin ('Dowex 50', H⁺), and chromatographed on paper using the following solvents: (1) ether–benzene–formic acid–water (50 : 50 : 12·5 : 2); (2) *n*-butanol–glacial acetic acid–water (100 : 6 : 25); (3) *n*-butanol saturated with 1·5 *M* ammonia. In each case, only one radioactive spot was found on the paper, which corresponded exactly with the location of the β-hydroxybutyric acid spot.

Cell-free extracts of *R. rubrum* also rapidly incorporate the β-hydroxybutyryl moiety of the coenzyme *A* derivative into polymer. As in *B. megaterium*, the activity is largely associated with the particulate fraction. The kinetics of incorporation are, however, complicated by the presence of an active depolymerase which is also associated with the particles. Crude extracts were prepared by sonic oscillation of cells grown anaerobically in the light. The particulate and supernatant fractions were separated by low-speed centrifuging. The former, which contained the polymer particles, was heavily contaminated with pigmented cell debris. The native polymer, when resuspended in either the supernatant fraction or buffer, underwent rapid hydrolysis to β-hydroxybutyric acid. As much as 80 per cent of the polymer disappeared after 30 min. of incubation at 33° C.

The results of an experiment in which labelled β-hydroxybutyryl-coenzyme *A* was added to a crude cell-free preparation are shown in Fig. 1. Maximal incorporation was achieved within 2 min., after which time the total carbon-14 content of the polymer rapidly decreased. The early termination of incorporation can be plausibly ascribed to exhaustion of the substrate. Thereafter, radioactivity is lost from the polymer as a consequence of the continued depolymerization. The results of a parallel experiment, in which the resuspended particulate fraction was incubated with different concentrations of substrate, are entirely compatible with this interpretation (Table 2). The identification of the carbon-14-labelled product was carried out as described above in the experiments with *B. megaterium*.

No direct activation of β-hydroxybutyric acid with adenosine triphosphate and coenzyme *A* could be demonstrated in cell-free extracts of *R. rubrum*. A small incorporation of carbon-14 into polymer was

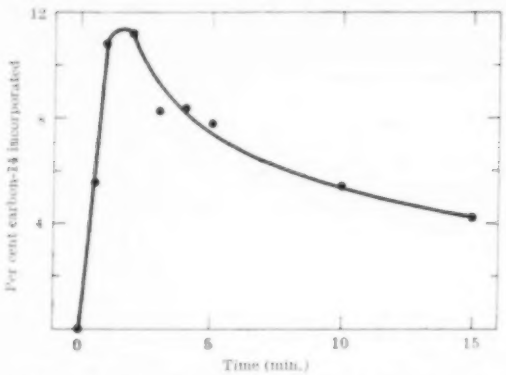

Fig. 1. Incorporation of carbon-14 into polymer by crude extracts of *R. rubrum*. The reaction mixtures contained crude extract (3·9 mgm. polymer and 5·08 mgm. protein per ml.); D(−)-β-hydroxybutyryl-coenzyme *A*, 1·4 μequiv.; and the following components (in μmoles per ml.): magnesium chloride, 12·7; glutathione, 12·7; and *tris* (hydroxymethyl) aminomethanehydrochloride buffer, *p*H 7·4, 127. The reaction mixtures were incubated at 33° C.

observed, however, when crude extracts were incubated with carbon-14-labelled acetate, adenosine triphosphate, coenzyme *A* and reduced pyridine nucleotides.

Two soluble enzymes, presumably involved in polymer metabolism, were found in the supernatant fraction of *R. rubrum* extracts prepared from cells that had depleted their polymer stores. A hydrolytic system catalyses digestion of boiled polymer particles of *R. rubrum* and native polymer particles of *B. megaterium* but does not attack the purified polymer. A specific diphosphopyridine nucleotide-linked D(−)-3-hydroxybutyric acid dehydrogenase is also present in such extracts, and has been partially purified.

Table 2. SYNTHESIS OF POLYMER BY PARTICULATE FRACTION OF *R. rubrum* EXTRACTS

Time (min.)	Percentage carbon-14 recovered in polymer fraction		
	Exp. 1	Exp. 2	Exp. 3
2	9	10	7
5	6	9	8
10	5	7	11

The reaction mixtures contained resuspended particulate fraction (3·1 mgm. polymer per ml.); and the following components (in μmoles per ml.): magnesium chloride, 10; glutathione, 10; and *tris* (hydroxymethyl) aminomethanehydrochloride buffer, *p*H 7·4, 100. Exps. 1, 2 and 3 contained 0·25, 1·0 and 4·0 μequiv. of D(−)-β-hydroxybutyryl-coenzyme *A* per ml. (initial), respectively. The reaction mixtures were incubated at 33° C.

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INHIBITION OF CELLULAR RESPIRATION BY CO-CARCINOGENIC FRACTIONS OF CROTON OIL

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As a result of the work of Rous and his colleagues[1] and Berenblum and his colleagues[2], it is widely accepted that carcinogenesis in skin—and probably also in other organs—takes place in two successive stages. A single small dose of a carcinogen such as 9 : 10-dimethyl-1 : 2-benzanthracene applied to mouse skin is sufficient to produce a lasting 'initiation' but no tumours. Subsequent repeated application of croton oil gives rise to a large crop of tumours, whereas croton oil applied without a previous initiating stimulus produces few, if any, tumours. Several arguments[3] make it clear that the 'promotion' or 'co-carcinogenesis' by croton oil is complementary to initiation and quite distinct from it; thus, administration of the initiator after prolonged treatment with croton oil does not lead to tumour formation.

The factor or factors in croton oil responsible for tumour promotion have not been identified, and their effects on cell metabolism have not previously been described. Lijinsky[4] has submitted methanolic extracts of croton seeds to silica-gel chromatography and obtained fractions, comprising about 1 per cent of the whole oil, that appear to have all its tumour-promoting activity. Fractions kindly provided by Dr. Lijinsky are at present being analysed by gas chromatography in this Institute in attempts to identify the active agent or agents. In the meantime, the opportunity has been taken—for reasons which will be apparent in the discussion here—to analyse the effects of the croton oil fractions on cell metabolism. It has been found that the highly active tumour-promoting fractions are inhibitors of cellular respiration in several tissues, and this property may well be related to their co-carcinogenic effect.

Rat liver homogenates. Livers of 100-gm. hooded rats were homogenized by the Potter–Elvehjem technique in the following medium: 0·3 *M* sucrose, 0·002 *M* sodium ethylenediamine tetraacetate and 0·03 *M* nicotinamide, adjusted to *p*H 7·1 with potassium hydroxide. Each Warburg flask contained 0·3 ml. homogenate (containing 1·02 mgm. protein nitrogen per ml.), 0·2 ml. potassium succinate, 0·15 *M*, *p*H 7·1 and 1·4 ml. sucrose–ethylenediamine tetraacetate–nicotinamide as above. Croton oil fractions were added in ten-fold dilutions in 0·05 ml. ethanolic solution to give final concentrations from 0·2 to 200 μgm. per ml. Oxygen uptake from air

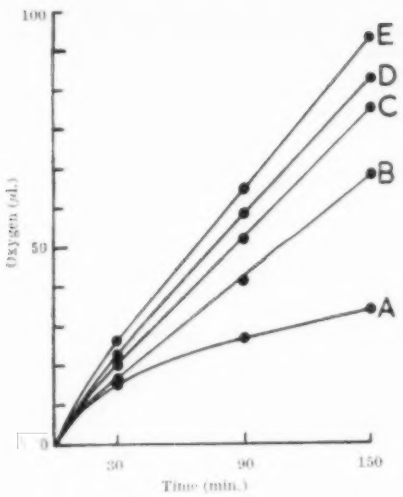

Fig. 1. Inhibition of oxygen consumption of rat liver homogenate with succinate as substrate by croton oil factor in various concentrations: *A*, 200 µgm. per ml.; *B*, 20 µgm. per ml.; *C*, 2 µgm. per ml.; *D*, 0·2 µgm. per ml.; *E*, no inhibitor

was measured in a Warburg apparatus for 2½ hr. at 30°. The results are shown in Fig. 1. Increasing concentrations of croton oil factor caused a progressive inhibition of respiration, up to 70 per cent inhibition at 200 µgm. per ml.

Rat liver mitochondria. Mitochondria were prepared from rat liver homogenates by five sedimentations and resuspensions in sucrose–ethylenediamine tetraacetate–nicotinamide medium. Each flask contained 0·3 ml. mitochondria (containing 0·33 mgm. protein nitrogen per ml.), 0·2 ml. sucrose–ethylenediamine tetraacetate–nicotinamide, 1·0 ml. reaction mixture and 0·1 ml. ethanol ± croton oil factor. A reaction mixture devised for prolonged oxidative phosphorylation in rat liver mitochondria was used, giving final concentrations per ml. of: 100 µmol. sucrose, 40 µmol. potassium chloride, 20 µmol. nicotinamide, 1·3 µmol. ethylenediamine tetraacetate, 10 µmol. potassium succinate, 20 µmol. potassium phosphate, 4 µmol. adenosine monophosphate, 0·5 µmol. diphosphopyridine nucleotide, 20 µmol. glucose, 4·6 k*M* units hexokinase and 8 µmol. magnesium sulphate, *p*H 7·1. Oxygen uptake from air at 30° measured in the Warburg apparatus is shown in Fig. 2. The croton oil factor at a final concentration of 100 µgm. per ml. inhibited respiration by 70 per cent.

Mouse skin. Since most of the experiments on co-carcinogenesis by the croton oil factor have been carried out in mouse skin, the effect of the factor on respiration of mouse ear tissues—the metabolism of which is due mainly to skin—was investigated. Four young adult Swiss mice were used. To one ear of each mouse 50 µgm. of croton oil factor in benzene was applied, and to the other ears benzene alone. Four hours later, the animals were killed by dislocation of cervical vertebræ. The ears were cut up into small pieces about 1 mm. square. The pieces from the control ears were placed in two Warburg flasks containing 2·5 ml. Earle's solution with *M*/30 *tris*-(hydroxymethyl)aminomethane buffer, *p*H 7·4, and 0·05 ml. ethanol. The pieces from the ears treated with the croton oil factor were similarly prepared, except that the ethanol contained a solution of the factor, the final concentration of which was 100 µgm. per ml. Oxygen uptake from air was measured in a Warburg apparatus for 2½ hr. at 30°. After the experiment, excess moisture was removed from the tissues by blotting with filter paper; the tissues were weighed, and oxygen uptake corrected for weight. In both flasks containing the croton oil factor oxygen consumption was less than in control flasks, the inhibition being 46 and 52 per cent. These results suggest that respiration in skin, as in other tissues, is inhibited by the croton oil factor.

Heart muscle succinoxidase preparation. The activity of croton oil fractions on a heart muscle sarcosome preparation was also investigated. The method of preparation of material, spectroscopic observation of cytochrome oxidation and reduction and estimation of succinic dehydrogenase using the Thunberg technique were as previously described[6]. Measurements of oxygen utilization in the determination of succinoxidase and cytochrome oxidase activities were made polarographically with a continually cleaned silver electrode in a 3-ml. chamber completely filled to exclude air[7]. Succinoxidase activity was measured in the presence of *M*/50 sodium succinate in 0·14 *M* potassium phosphate buffer, *p*H 7·3. Cytochrome oxidase was measured in the presence of 0·05 *M* *p*-phenylenediamine and 0·14 *M* potassium phosphate buffer, *p*H 7·3. No additional cytochrome *c* was added, and all experiments were carried out at 30°. The final concentration of the heart muscle preparation used was 2·4 mgm. per ml.

Visual observation of the cytochrome absorption bands showed that the croton oil factor at a concentration of 100 µgm. per ml. inhibited the reduction of cytochromes *a* and *c* and the oxidation of cytochrome *b*. The inhibitory effect of various concentrations of the croton oil factor on overall succinoxidase activity is shown in Fig. 3. At a concentration of 50 µgm. per ml. there was also some inhibition of cyto-

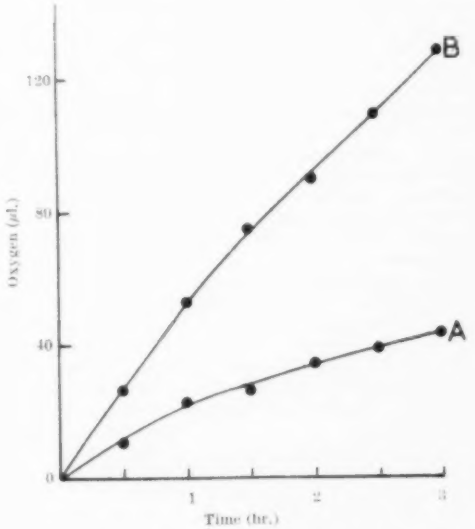

Fig. 2. Inhibition of oxygen consumption of rat liver mitochondria with succinate as substrate by croton oil factor. *A*, inhibitor at a concentration of 100 µgm. per ml.; *B*, no inhibitor

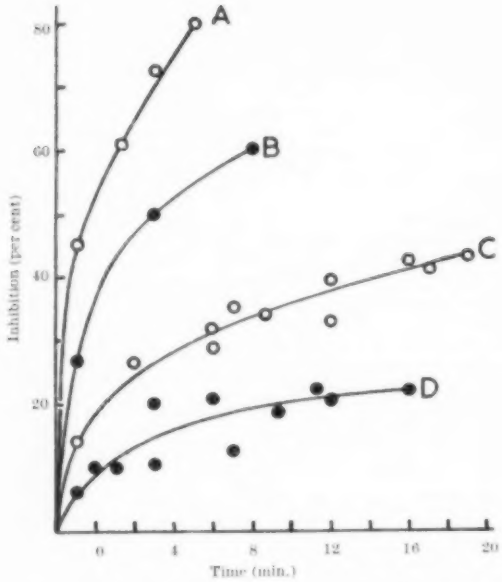

Fig. 3. Inhibition of heart muscle succinoxidase preparation by croton oil factor in various concentrations: *A*, 150 μgm. per ml.; *B*, 100 μgm. per ml.; *C*, 50 μgm. per ml.; *D*, inhibition of cytochrome oxidase by croton oil factor at 50 μgm. per ml.

chrome oxidase, but no inhibition of succinic dehydrogenase. These observations show that the croton oil fraction used has several points of resemblance with antimycin *A* (ref. 8) and quinoline-N-oxide[9] in its metabolic effects. This pattern of inhibition has been shown to indicate a block in electron transport between cytochromes *b* and *c*. The inhibitory effect of the croton oil factor, however, developed more slowly than that produced by antimycin *A* and quinoline-N-oxide, and only the croton oil is also slightly inhibitory of cytochrome oxidase.

In general, the observations we have made suggest that the croton oil factor produces an overall inhibition of terminal respiration mediated through cytochromes. It seems unlikely that the effects reported here are due to alteration of the structural integrity of the cellular particles concerned. Phase-contrast microscopy of rat liver mitochondria exposed to 100 μgm. per ml. of the croton oil factor showed no detectable abnormality. At concentrations of the factor producing marked inhibition of overall succinoxidase activity there was much less inhibition of cytochrome oxidase and no detectable inhibition of succinic dehydrogenase activity.

The results described here show that fractions of croton oil having powerful co-carcinogenic activity contain inhibitors of terminal cellular respiration mediated through cytochromes that are effective in several tissues. It has been found that 100–200 μgm. per ml. of the croton oil fractions produce 70–80 per cent inhibition of respiration in liver and heart muscle preparations. When it is recalled that these fractions are still impure, and that owing to their lipid solubility penetration into tissues in aqueous suspension is poor, it seems likely that the factor or factors inhibiting respiration are highly active. They certainly produce detectable respiratory inhibition in skin at concentrations used for tumour promotion.

The only other metabolic effects of purified croton oil fractions so far described concern active transport of glucose by the isolated surviving guinea pig intestine[9]. The croton oil fractions were found to depress absorption of glucose under aerobic conditions to that observed under anaerobic conditions; absorption under anaerobic conditions was not affected by croton oil, and other oils were without effect. An interpretation of these results consistent with our own findings is that croton oil depressed the yield from oxidative phosphorylation of adenosine triphosphate required for active transport of glucose. The yield of adenosine triphosphate from glycolysis was not apparently diminished by croton oil, which confirms our impression that the main inhibition is on terminal respiration, with little, if any, effect on other enzyme systems.

It is not yet established that the two properties of croton oil fractions, namely, respiratory inhibition and co-carcinogenesis, are related, but available evidence suggests that they may be. It is well known that tumour cells have high rates of aerobic as well as anaerobic glycolysis[10–12]; tumour cells are also able to use very efficiently adenosine triphosphate derived from glycolysis for protein synthesis[13]. It might therefore be expected that respiratory inhibition would retard growth and division of tumour cells less than that of normal, differentiated cells. In the mouse skin system which has been used for most work on co-carcinogenesis, this supposition seems to be well founded. There is substantial evidence that energy from oxidative phosphorylation is required for division of normal mouse skin cells[14], whereas preliminary results suggest that mouse skin papilloma cells continue to divide when cultured in an atmosphere of nitrogen and carbon dioxide in the presence of adequate glucose (Allison, A. C., unpublished work).

Promotion of co-carcinogenesis can therefore be envisaged as a process by which small numbers of tumour cells (produced by the initiator or carcinogen) are placed at a competitive advantage over normal cells the growth of which is handicapped by respiratory inhibition. Under the continued influence of the promoter, then, it can be supposed that tumour cells can form clones sufficiently large to become self-perpetuating. Experiments with other respiratory inhibitors are in progress to test this hypothesis further.

It should be noted that this hypothesis of carcinogenesis is the opposite of that proposed by Warburg[10]. According to Warburg, cancer cells are formed in two distinct stages: an irreversible lesion of cell respiration comes first; as a result, some cells die but others become capable of replacing respiration by glycolysis as the main energy-producing reaction and are changed into cancer cells. However, careful search has failed to show substantial impairment of oxidative phosphorylation in tumour cells and mitochondria, and the general conclusion, discussed in detail by Weinhouse[11] and by Schlief and Schmidt[12], is that the high aerobic glycolysis of cancer cells is much less the result of a lesion in respiration than of an enhancement of glycolysis. The evidence thus supports our view that an early change in tumour cells is increased glycolysis, releasing the cells from strict dependence on energy derived from oxidative phosphorylation for growth. The phase of respiratory inhibition does not act directly on tumour cells, as Warburg supposed, but acts as a selective inhibitor of normal cells.

An attractive feature of this hypothesis of co-carcinogenesis is that it not only embraces the effects of anoxia from various causes but can also be extended to include co-carcinogenesis by viruses. Andrewes *et al.*[15] reported that when the fibroma virus—which normally produces benign, regressing lesions—was given to rabbits injected subcutaneously with tar, sarcomata were formed; no tumours were obtained with tar alone. Duran-Reynals[16] produced epitheliomata in the skins of fowls infected with fowl-pox virus and treated with sub-carcinogenic doses of methylcholanthrene; and Rous *et al.*[17] have shown that when the papilloma virus is given to rabbits, the skins of which had been treated with tar, malignant tumours develop rapidly. The nature and timing of the responses in these experiments indicate that the viruses (one of which, fowl-pox, is not a tumour virus at all) are acting as co-carcinogens, their effects being complementary to those of the carcinogens, tar and methylcholanthrene.

A common metabolic pattern in virus-infected cells is increased glycolysis[18], and, if there is competition for phosphate acceptors within the cells as envisaged by Chance and others[19], this would result in respiratory inhibition. Some of the metabolic effects in virus-infected tissues are probably due to interferon, which has been shown to increase glycolysis when added to cells[20]. Indeed, Isaacs[21] has already suggested that interferon may produce conditions favourable for the growth of tumour cells, and so act as a promoter. Increased aerobic glycolysis is a prominent feature of cells infected with the Rous sarcoma virus[22] and the mouse polyoma virus (Allison, A.C., unpublished work), so there is little doubt that these viruses can act as powerful promoters. Whether the tumour viruses—perhaps in contrast to other viruses—can also act as initiators remains to be determined.

We are indebted to Dr. W. Lijinsky for supplying purified croton oil fractions, to Dr. D. B. Roodyn for co-operation in some experiments and to Dr. A. Isaacs for helpful discussion.

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MORPHOLOGICAL CHARACTERIZATION OF THE VIRUS OF THE HUMAN COMMON WART (*VERRUCA VULGARIS*)

By M. G. WILLIAMS, A. F. HOWATSON and J. D. ALMEIDA
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IT is now more than ten years since Strauss *et al.*[1,2] published electron micrographs showing arrays of particles of average diameter 52 mμ in shadowed preparations of extracts obtained from human warts. These particles were believed to be the causative agent of certain types of human warts. Further evidence for the presence of specific particles in human wart tissue was obtained shortly afterwards by Bunting *et al.*[3], who were able to demonstrate arrays of particles within the nuclei of epidermal cells by using the newly developed thin-sectioning technique. The diameters of the particles seen in sections were in the range 20–38 mμ. The smaller size in sections was attributed to differences in preparative procedures. Although techniques for the morphological characterization of viruses have improved considerably since these investigations were carried out, little or no new information about the human wart virus has apparently been obtained. In a recent article, however, Siegel[4] has questioned the conclusion of Strauss *et al.* that the 52-mμ particles represent the human wart virus and has suggested that particles of diameter 16 mμ seen in his shadowed preparations are the causative agent.

In the present article, we describe observations on thin sections of human wart tissue, and on extracts of warts prepared for electron microscopy by the negative staining and shadow-casting techniques. By all three methods numerous particles of well-defined morphology were demonstrated, the most detailed characterization of the particles being obtained by the negative staining method.

Four common warts clinically typical of *verruca plana* and *verruca vulgaris* were examined by the thin-sectioning method. In three of these, the nuclei of some cells in the granular layer, close to the keratin layer, contained uniform particles of mean diameter 46 mμ. Most of the particles consisted of a dense core of diameter 34 mμ surrounded by a less-dense layer of width about 6 mμ, but in some the central region was less dense than the periphery. Fig. 1 illustrates the appearance of a typical group of particles. In one specimen the particles were for the most part arranged in close-packed crystalline formations; but in the others they were scattered at random throughout the nucleus. No particles were seen in the cytoplasm of any of the cells.

Two extracts were prepared, one from eight warts removed from several patients, the other from two warts obtained from two different patients. The warts were ground in a mortar with sand and distilled water and the homogenate clarified by

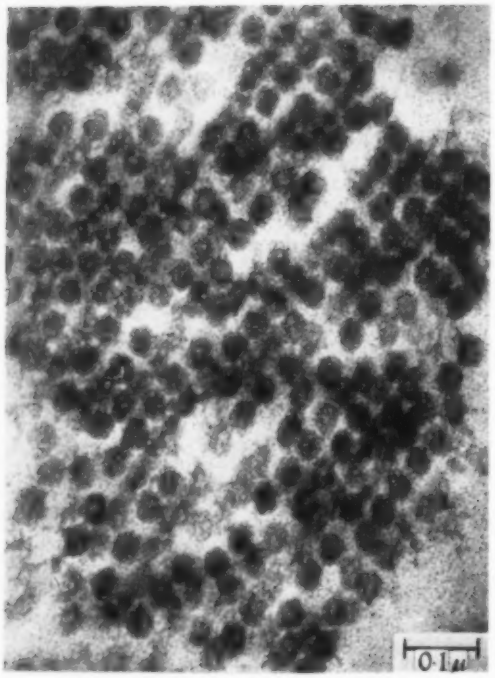

Fig. 1. Thin section showing part of an intranuclear aggregate of virus particles in a cell from the granular layer of a human wart

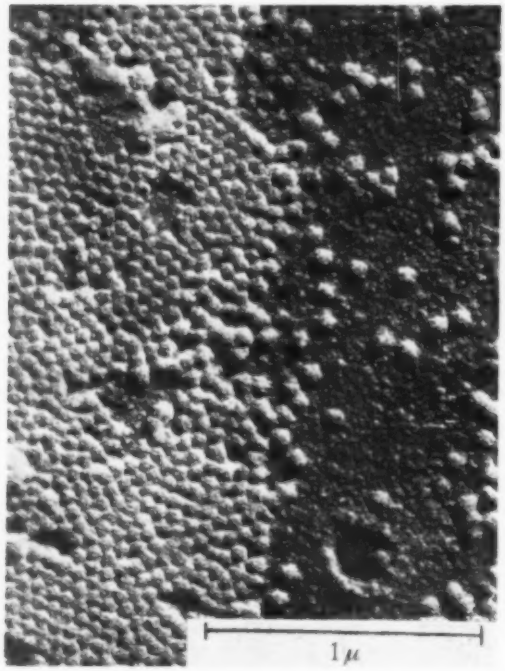

Fig. 2. Shadowed preparation from extract of human warts showing particles both scattered and in close-packed array

low-speed centrifugation. The supernatant was then centrifuged at 35,000 *g* for 2 hr., and the sediment from this centrifugation, re-suspended in a small volume of distilled water, formed the extract. Samples of extracts from both pools of warts were prepared for examination in the electron microscope by standard shadowing techniques, using gold-palladium alloy, and also by the negative staining method[5], using phosphotungstic acid brought to a *p*H of 5·4 with sodium hydroxide.

In shadowed preparations most of the specimen material present on the grid was in the form of particles similar in size and appearance to those described by Strauss *et al.*[1,2]. Fig. 2 shows a typical field. The average diameter of particles in close-packed array is 55 mμ. Isolated particles appear appreciably larger, most having a diameter in the range 65–75 mμ. We were unable to detect the 16-mμ particles described by Siegel[4] in our preparations.

Specimens prepared by the negative staining method provided convincing evidence that the particles present in large quantities in our preparations were, indeed, viruses. By this method, it is apparent that the surfaces of the particles are composed of symmetrically arranged sub-units similar to those that have been described for other viruses[6,7]. Fig. 3*a*

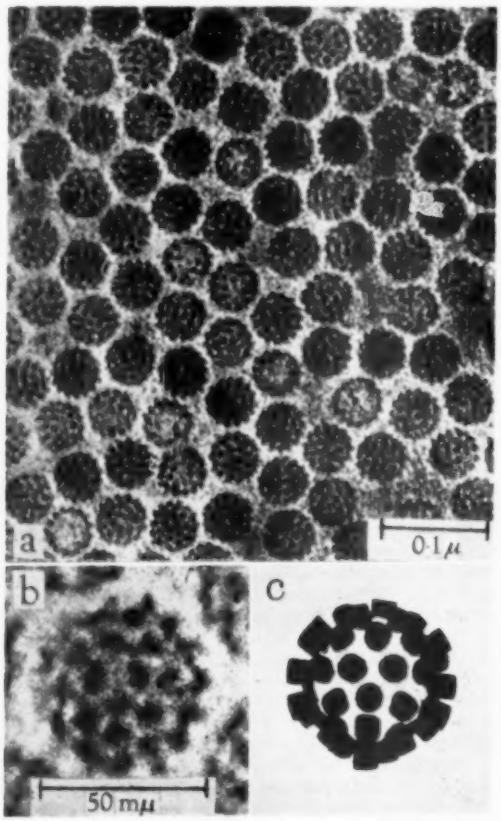

Fig. 3*a*. Portion of an aggregate of virus particles treated with phosphotungstic acid. Symmetrically arranged sub-units are visible on the surfaces of the particles; *b*, single virus particle at high magnification; *c*, model in same orientation as particle showing close correspondence in arrangement of sub-units

shows a small portion of a large aggregate of particles. In Fig. 3*a*, reproduced from a negative print, the sub-units appear dark against a light background. From observations of the arrangement of the sub-units or capsomeres on particles on which they are particularly distinct, it has been deduced that the shell or capsid of the particle consists of 42 capsomeres arranged in 5 : 3 : 2 axial symmetry. Twelve of the capsomeres are situated at the vertices of a regular icosahedron, and the remaining 30 are at the mid-points of the edges between adjacent triangular faces. The capsomeres have a diameter of approximately 8 mμ and are separated from one another by a distance of about 4 mμ. The overall diameter of the particles has an average value of 55 mμ. In Fig. 3*b* is shown an example of a particle in which virtually all the sub-units on one side of the particle are visible. Fig. 3*b* may be compared with Fig. 3*c*, which is a photograph of a model in the same orientation as the virus particle in Fig. 3*b*. In the negative-stained particle the peripheral capsomeres are more prominent than in the model, suggesting that the particle is somewhat flattened, but otherwise the correspondence between particle and model is close.

The number and arrangement of the capsomeres on the wart virus is the same as that established by Wildy *et al.*[7] for polyoma virus. The latter virus, however, is smaller, having a mean diameter of 45 mμ. It is of interest that the wart virus which produces a benign tumour in man is structurally similar to polyoma virus, which produces a wide spectrum of malignant tumours in several species of animals.

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HAPTOGLOBINS AND TRANSFERRINS OF TWO TROPICAL POPULATIONS

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THE haptoglobins are a family of serum proteins characterized by their ability to bind haemoglobin. They have been studied extensively since 1938 by Jayle *et al.*[1]. Smithies[2] found that human populations could be divided into three types, termed 1–1, 2–2 and 2–1, dependent on their haptoglobin patterns. It has since been shown that for many populations the haptoglobins are determined by two autosomal genes, Hp^1 and Hp^2. Homozygous Hp^1 individuals are type 1–1; homozygous Hp^2 are type 2–2; and heterozygotes are type 2–1[3]. The genetics, and other features of this trait, have been reviewed recently[4,5].

A particularly interesting phenotype is that in which no haemoglobin binding can be demonstrated. This type (designated *O*) is most common in West Africans[6], but it is also found in other populations[7–9]. There is, as yet, no adequate genetic explanation for this type. There is a striking difference in the distribution of the phenotypes in different populations[10]; and this is presumably due, in part, to differences in the selective forces which operate to maintain this genetic polymorphism. In this regard, it is interesting that there does not appear to be a polymorphism in some lower primates; a haptoglobin band which migrates with approximately the mobility of human haptoglobin type 1–1 was the only one found in a study of 170 *Macaca mulatta* monkeys, 4 chimpanzees, and 34 baboons[11]. Haptoglobin 2–1-like sera are, however, seen in some other species[11].

Transferrin (or siderophilin) is the iron-binding protein of serum. Most American White individuals have a single iron-binding band, termed transferrin *C*. However, in a small number of American Negroes, and in a larger number of Australian Aborigines, a second band, transferrin *D*, is found; and a fast-moving band, termed *B*, is found in some European and Asian populations. Smithies and Hiller[12] have demonstrated that the transferrins are genetically controlled at a single locus *Tf* by at least three alleles, Tf^B, Tf^C and Tf^D. Transferrins of intermediate frequency, termed B_1, B_2, D_1, D_2, D_3, have also been found, but their genetics is not yet completely determined.

During the 1959 health survey of the Micronesian inhabitants of Rongelap Atoll, Marshall Islands (who had accidentally been exposed to radiation fall-out in 1954[13]) blood samples were collected for haematological and other studies. An aliquot of the serum was made available for the present examination.

Rongelap is in the Ralik (Western) chain of the northern Marshalls at approximately 11° N. The inhabitants are Micronesians, an Oceanic group, who have affinities with Polynesians and Melanesians, and, presumably, remotely with inhabitants of south-east Asia. Serum was obtained from 176 individuals, representing 70 per cent of the inhabitants at the time of the visit. Also studied were 118 sera collected in Rongelap in 1957, and kept frozen since their collection. The 1959 collection included nearly all the individuals sampled in 1957.

The West African sera were collected from Nomadic (or Pastoral) Fulani in several regions of northern Nigeria (at approximately 12° N.) in the summer of 1957. The population studied is described in greater detail elsewhere[14]. The red blood cells and serum were separated shortly after collection, and the latter frozen until the haptoglobin and β-globulin determinations were made in 1959. We are indebted to Dr. Hayhurst, medical officer at Pankshin, Nigeria, for supplying 59 of the sera. In all cases, blood was removed by venipuncture and allowed to clot in a dry test-tube at room temperature. The serum was separated by centrifuging and pipetting.

Table 1. Distribution of Haptoglobin and Transferrin Types in Rongelap and Fulani Populations

Population	Haptoglobins								Transferrins					
	Total No.	1–1 No.	1–1 Per cent	2–2 No.	2–2 Per cent	2–1 No.	2–1 Per cent	0 No.	0 Per cent	Total No.	*CC* No.	*CC* Per cent	*CD* No.	*CD* Per cent	*DD* No.	*DD* Per cent
All Rongelap	176	59	33·5	31	17·6	83*	47·2	3	1·7	66‡	100	100	—	—	—	—
Rongelap, selected	124	41	33·1	18	14·5	62*	50·0	3	2·4	—	—	—	—	—	—	—
Fulani	84	24	28·6	4	4·8	14†	16·6	42†	50·0	68	57	83·8	10	14·7	1	1·5

* Includes one type 2–1 *M* ('type *F*' of Blumberg *et al.*) (ref. 7).
† Includes two sera in which only the fourth fastest band of type 2–1 was visible.
‡ In addition to the 66 sera studied by the *tris* discontinuous buffer method, 40 were studied by the horizontal borate method and found to be type *CC*.

We used the starch-gel electrophoresis method of Smithies[2], with borate buffer, and the conditions for serum described by him. Approximately 80 per cent of the sera, including all those of haptoglobin type *0*, were also run with the discontinuous (*tris*) buffer system of Poulik[15]. The haptoglobins were identified by adding human haemoglobin solution to an approximate concentration of 120 mgm. per 100 ml. to serum which was not already haemolysed, and staining for haemoglobin with benzidine and hydrogen peroxide[16]. Transferrins were determined by the discontinuous buffer system on 68 Fulani sera and 66 Micronesian sera. In addition, observations on an additional 40 Micronesian sera were made using the borate buffer, horizontal method. No types other than *CC* were seen in the Micronesian sera. All sera which were of phenotypes other than *CC* were also studied by the vertical borate method of Smithies[17]. In confirming the transferrin types of sera other than type *CC*, the position of the protein was confirmed by adding to the serum radioactive ferric chloride (obtained from Abbott Laboratories, Oak Ridge, Tennessee) to a final concentration of approximately 3×10^{-5} molar iron, and subjecting the resulting mixture to electrophoresis in the usual manner. Radioautographs of one-half of the slit gel were made by the method described by Blumberg and Robbins[18].

The distribution of the haptoglobin types in the 176 Rongelapese tested is shown in Table 1. This sample includes some families in which two or more offspring are included. In these, all but one sibling were removed by random selection. This resulted in a sample of 124 individuals in which, at most, the parents and one child of a family were included. The distribution of the haptoglobin types in this group did not differ significantly from that in the entire group. In each case, agreement with the Hardy–Weinberg predictions was good, suggesting that the population was homogeneous for this trait. Omitting the three sera with no haptoglobins, the frequency of the Hp^1 gene is 0·58 and of the Hp^2 gene is 0·42. The frequency of the Hp^1 gene is higher than in European populations so far tested.

There were four Rongelapese who had no detectable haptoglobin, either in 1957 or 1959. In addition, there were many sera in which very small amounts only of haptoglobin were visible. This included two which were very faint 2–2's, but in which the fastest-moving haptoglobin band was not seen.

There were two sera (30, 830) which had no detectable haptoglobin, both in 1957 and 1959; in a third (933) only a 1959 serum was available, and this was ahaptoglobinæmic. One serum (842) was a very faint 2–2 in 1957, but ahaptoglobinæmic in 1959. Another (822) was a faint 2–2 in 1957, and in 1959 had a barely detectable amount of haptoglobin, which could not be typed. There was one individual (882) who had a pattern in which the fast-moving haptoglobin band of type 1–1, and the second fastest-moving haptoglobin band of a type 2–1 was present. This is similar to the 'type 2–1 *M*' described by Smithies and Connell[4], which appears to be identical with the 'type *F*' pattern of Blumberg *et al.*[7]. The pedigree of the family with the unusual types is shown in Fig. 1.

The Micronesian sera studied were all transferrin type *CC*. This includes 66 studied by the *tris* discontinuous buffer method and 40 by the horizontal borate buffer method.

The distribution of the haptoglobin types in the Fulani is shown in Table 1. More than half had no detectable haptoglobin, the highest frequency of this type yet reported. Included in the ahaptoglobinæmic sera were two in which only a single band corresponding to the fourth fastest moving band of type 2–1 was visible. This variant had not been seen in any previous studies. Of those who could be typed, nearly 60 per cent were type 1–1, and only four were type 2–2. 15 per cent of the 68 sera had both transferrin *C* and *D*, and one of them had only transferrin *D* (Table 1). Assuming that the genetic hypothesis of Smithies is correct, the distribution of the phenotypes is consistent with the Hardy-Weinberg prediction; and the frequency of the Tf^D gene is 0·1. The serum of the single *D* phenotype was used in studies on the chemical structure of the transferrin to be reported elsewhere[19]. All the slow-moving transferrins had

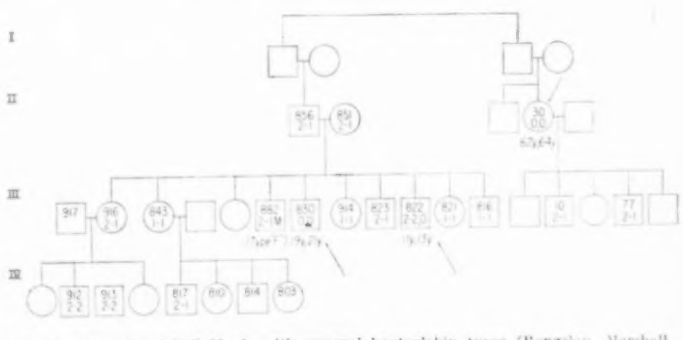

Fig. 1. Kinship of individuals with unusual haptoglobin types (Rongelap, Marshall Islands)

The results of the studies on the 1957 and 1959 sera are shown for those individuals with ahaptoglobinæmia

identical mobility, and no fast-moving transferrins were found.

Considerable caution must be exercised in extrapolating to an entire population the gene frequencies obtained from a small sample. This is particularly true when studying societies made up of small isolated or semi-isolated groups in which genetic drift might be expected to operate. Thus, the Rongelapese appear to have a fairly high frequency of type 1-1. However, this may not be the case for all the Marshall Islands. Approximately 60 sera were obtained from each of two other Marshall Islands, Majuro and Utirik. In each of these the frequency of type 1-1 was lower than in Rongelap and closer to the European frequency.

Most of the Fulani sera which could be typed were of type 1-1, and the frequency of the Hp^2 gene was very low indeed. This is consistent with other findings from West Africa[6,20], in which as many as 50 per cent of the samples were of type 1-1. The frequency of Fulani with no haptoglobin is, to our knowledge, the highest yet reported. Each of the *O* types was re-checked two or more times, using the *tris* buffer, and, in addition, approximately half of them were re-checked using the vertical gel method with borate buffer. Only those in which there was no benzidine staining material in the region of the haptoglobins were scored as type *O*.

It is clear from the Micronesian studies that, at least in some cases, an individual may have no haptoglobin at one point in time, but have sufficient haptoglobin to permit typing at another time. (In this case, the interval of sampling was two years.) A complete medical and physical examination and determination of the haemoglobins, red blood counts, white blood counts, and haematocrit were performed on all the ahaptoglobinaemic individuals on Rongelap. No abnormalities which might differentiate them from individuals with typable haptoglobin were noted. Both the individuals, who at one time were typable and at another were ahaptoglobinaemic, were of phenotype 2-2. This was also true in the two cases reported by Galatius-Jensen[9]. However, Sutton *et al.*[10] reported a single individual who was at one time ahaptoglobinaemic but who could later be typed as a 2-1. A further case in point is a patient studied by Shulman and Blumberg[21]. A five-year-old schoolboy developed a haemolytic anaemia due to the presence of Donath-Landsteiner cold haemolysis, of unknown aetiology. There were two acute episodes of haemolysis within 48 hr., but no further evidence of clinical haemolysis after this. One week after the initial haemolytic episode, there was no detectable haptoglobin in the boy's serum. One month later, 2 bands corresponding to the second and third fastest bands of type 2-2 were detected. These bound approximately 20 mgm. of haemoglobin per 100 ml. of serum. Three months after the initial haemolytic episode, the patient had a normal 2-2 pattern which bound 120 mgm. of haemoglobin per 100 ml. of serum, approximately a normal amount. However, retesting the serum of the patient one year after the original haemolysis again failed to detect any haptoglobin despite the fact that there had been no clinically detectable haemolysis in the interim. Apparently the patient had been intermittently ahaptoglobinaemic and in one case without regard to the presence of the haemolytic episode. The patient's mother was a type 2-2, but bound an abnormally low amount of haemoglobin (approximately 20 mgm. of haemoglobin per 100 ml. of serum).

The ahaptoglobinaemia kinship (Fig. 1) does not help to elucidate the genetics of this type. One of the sibs of an ahaptoglobinaemic was a type 2-1 *M*. Giblett[22] has reported that many ahaptoglobinaemic children were born to matings in which at least one parent had the phenotype 2-1 *M*.

An explanation of the ahaptoglobinaemic type is still not available. In some cases, at least, it appears to vary during life; and it is known that most infants do not have haptoglobin. The familial clustering, and the association with the 2-1 *M* type, suggest that some inherited factor is involved. The most probable explanation is that there is an inherited propensity to develop ahaptoglobinaemia, and that under different environmental conditions, ahaptoglobinaemia may develop. Under extreme conditions, such as severe haemolytic anaemia, any individual could develop ahaptoglobinaemia. It is known that other pathological conditions such as liver disease, uraemia and Addison's disease can also lead to a decrease in haptoglobins.

The relatively high frequency of the transferrin types *CD* and *DD* in the Fulani is consistent with the findings in other African groups[23]. On the basis of the small number studied, this appears to be among the highest frequencies found in Africa, and is second only to the prevalence in Australian Aborigines. The complete absence of transferrin *D* in the Micronesian sample is in interesting contrast to the findings on the Fulani. There is no evidence as to what forces maintain this polymorphism in some but not other populations.

We are grateful to Dr. R. A. Conard, leader of the Brookhaven National Laboratory medical survey team to Rongelap, for his assistance in securing the Micronesian blood samples and for his encouragement and help in the conduct of this work. Some of the Fulani blood samples were collected during an expedition to Nigeria supported in part by the Wenner-Gren Foundation, Inc. Mr. O. Oyefesu, Ibadan, assisted in the collection of the Fulani samples.

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MODE OF ACTION OF AN ANTHERIDIUM-INDUCING SUBSTANCE IN FERNS

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THE control of antheridium formation in certain fern species by a naturally occurring substance[1,2] has been reviewed before in detail[2]. The substance is specifically concerned with the formation of male sex organs in many species of the family Polypodiaceæ and the representative tested of the family Dicksoniaceæ, while the species investigated of some other fern families (Cyatheaceæ, Osmundaceæ, Schizaeaceæ) are unresponsive to it[1,2].

The prothalli of *Onoclea sensibilis* and *Pteridium aquilinum* form antheridia in response to the active substance only during an early phase of development. They become insensitive to it soon after they become heart-shaped, and a few days prior to attaining the archegonial phase. Once insensitive, the *Onoclea* prothalli fail to form antheridia even if supplied with the substance at a concentration 15,000 times as high as that sufficient to induce antheridia in prothalli just two days younger[6]. Soon after the prothalli of *P. aquilinum* and of many other polypodiaceous fern species attain the archegonial phase, the last of the ephemeral antheridia formed during the sensitive phase disintegrate.

Czaja[7] and Dopp[8] observed that meristemless fragments excised from the archegonium-bearing prothalli of *Blechnum brasiliense* and of *P. aquilinum*, respectively, proceeded to form antheridia again. Demeristemized, archegonium-bearing *Onoclea* prothalli which were cultured on medium supplemented with antheridial factor also gave rise to antheridia[3]. It has already been mentioned that the archegonium-bearing prothalli of this species are no longer responsive to the antheridial factor. The re-appearance of antheridia in the meristemless fragments shows that the loss of sensitivity to the active substance is maintained as a function of the meristematic region.

Further investigations which were carried out on wings (meristemless fragments), excised from 24-day-old (insensitive) prothalli and cultured on medium containing antheridial factor, showed that the lag period between excision and the first appearance of antheridium initials varied considerably, ranging from 7 to about 14 days[3]. In contrast, most intact prothalli responded to the antheridial factor within 2½–3½ days while they were still at the sensitive stage. Thus the wings excised from the insensitive prothalli formed antheridia with considerable delay. This delay cannot be ascribed to damage incurred by excision because regenerative cell division could be clearly discerned within one day in a few of the wings and within two days in a majority of them. The delay may be understood, however, if we assume that the restoration of sensitivity to the antheridial factor follows excision not abruptly but gradually. Further observations indicated that antheridia arose only in those regions of the regenerating wings that had first undergone a number of vegetative cell divisions[3]. Perhaps, therefore, sensitivity to the antheridial factor is restored as a function of regenerative cell division.

It could be further observed that many excised wings gave rise to antheridia even on medium not supplemented with the antheridium-inducing substance. This is quite surprising if we consider that intact prothalli of this species fail to form antheridia spontaneously under the prevailing conditions of culture[2].

This observation suggests the possibility that meristemless fragments give rise to antheridia without the intervention of the antheridial factor. In turn, such an assumption leads to the hypothesis that the antheridial factor acts by overcoming a block to antheridium formation that is imposed on the prothallus by the meristematic region.

The hypothesis implies that this block to antheridium formation is operative as soon as the prothallus responds to the antheridial factor, that is, at a very early stage of development. In contrast, the prothalli do not become insensitive to the antheridial factor until after they have attained heart shape. The postulated reversibility by the antheridial factor of the newly proposed block also contrasts with the finding that the loss of sensitivity cannot be reversed by that factor[6]. The two phenomena should therefore be treated as distinct events in the development of the *Onoclea* gametophyte.

The present report is concerned with an attempt to put the proposed hypothesis to an experimental test.

The procedures used in the sterilization and inoculation of the spores have been described elsewhere[4,5]. A detailed description of the conditions of culture has also been given. The prothalli were cultured in 50-ml. flasks which contained 10 ml. of the mineral medium solidified with 1 per cent agar. Antheridium-inducing activity was assayed against prothalli of *O. sensibilis* by means of a dilution series. The prothalli of this species proved ideal for this purpose because they failed to form antheridia spontaneously under the prevailing conditions of culture, but formed them readily if the medium was supplemented with antheridial factor[2]. The active substance was supplied as the diluted liquid medium from 7-week-old cultures of *P. aquilinum*, which was commonly active to a dilution of 1 : 30,000 (ref. 2).

With the proposed hypothesis in mind, the formation of antheridia by demeristemized prothalli was studied more closely. Two hundred wings (that is, meristemless parts of the gametophytes) were excised from 16-day-old *Onoclea* prothalli and transferred to new medium in 50-ml. flasks that was supplemented with antheridial factor (supplied as 1:100 full strength *Pteridium* medium that elicited an antheridial response to a dilution of 1 : 30,000). Another 200 wings were transferred to medium not supplemented with antheridial factor. Five wings were cultured in each 50-ml. flask. Samples of 20 regenerating fragments were then examined for the presence of antheridia at intervals of one

Table 1. Formation of Antheridia by Excised Wings on Medium with and without Antheridial Factor

Days after excision	Plus antheridial factor		Minus antheridial factor	
	No. of wings with antheridia	No. of wings with archegonia	No. of wings with antheridia	No. of wings with archegonia
4	0	0	0	0
5	0	0	0	0
6	1	1	0	0
7	5	1	3	1
8	7	2	5	3
9	9	3	8	4
11	11	4	10	6
13	14	8	11	8
15	15	10	9	12
17	13	14	7	17

day or, at later stages of regeneration, at intervals of two days. These observations were continued until the number of antheridium-bearing fragments began to decline. This decline occurs because the regenerating fragments stop forming antheridia when they attain the archegonial phase, as is the case with the prothalli of most polypodiaceous species.

Table 1 shows that the maximal counts of antheridium-bearing regenerates never reach twenty, that is, the number of wings examined at each interval. This indicates that some of the regenerating wings lack an antheridial phase. It seems possible, however, that the antheridia observed on the regenerating wings with an early male phase disintegrate before other regenerates attain this reproductive phase. Thus, the data of Table 1 seem equally consistent with the assumption that all the excised wings form antheridia.

Fifty wings that bore antheridia only 10 days after excision were returned to the medium and re-examined seven days thereafter. Thirty-eight of the fragments then bore 1–4 archegonia. All regenerates with one or two archegonium initials and three out of five wings with three such initials then still bore antheridia. In contrast, the lone fragment which had already given rise to the fourth archegonium lacked antheridia. Whereas these results pertain to wings cultured on medium supplemented with antheridial factor, it was demonstrated that on unsupplemented medium the last-formed antheridia also persist until at least two archegonia have been initiated. The regenerating *Onoclea* wings behave similarly in this respect to intact prothalli of *P. aquilinum*[5].

The wings which attained the archegonial phase up to 11 days following excision in the presence of antheridial factor, or up to 13 days following excision in its absence, invariably lacked antheridia even if they had initiated only the first archegonium. Bisexual wings first appeared among the 20 wings examined two days thereafter. (This is reflected in the fact that the sum of antheridium-bearing and of archegonium-bearing wings then surpasses 20 for the first time; see Table 1.) Their number increased in the samples examined afterwards, and bisexual wings with up to three archegonial initials could then be seen. It may be concluded that among wings exposed to antheridial factor approximately four wings (that is, the number of wings that have reached the archegonial phase prior to the first appearance of bisexual wings; see Table 1) to about five wings (that is, 20, the number of wings examined per interval, minus 15, the maximal count of antheridium-bearing wings) out of 20 failed to form antheridia. Based on these same considerations, it is inferred that, among wings not exposed to antheridial factor, about eight or nine out of 20 attained the archegonial phase without a prior antheridial phase. The available data thus permit the conclusion that the maximal counts of antheridium-bearing wings reflect accurately, or with little error, the proportion of wings with an antheridial phase.

As already stressed, the maximal count of antheridium-bearing wings is higher in the presence of antheridial factor (15 out of 20) than in its absence (11 out of 20). The difference was even more pronounced in three repetitions of this experiment. The conclusion was drawn that the addition of the antheridial factor increases the proportion of antheridium-forming regenerates. Table 1 further shows that the first antheridium-bearing fragment appears one day earlier in the presence of antheridial factor than in its absence. Results of the three repetitions are in agreement with the conclusion that antheridium-bearing wings can be seen earlier in the presence of the antheridial factor than in its absence.

Fragments regenerating in the presence of antheridial factor may give rise to antheridia in the interval following the decay of the loss of sensitivity imposed on the wing by the meristem of the mother prothallus and prior to its re-imposition by a newly regenerated meristem. Thus, the regenerates with an early archegonial phase (those with the most rapid rate of regenerative development) would seem to lack an antheridial phase despite the presence of the active substance because this interval is too brief or non-existent.

In the absence of the factor, the phase of regenerative development conducive to antheridium formation is, in the context of the hypothesis, expected to be still briefer if it is recalled that the postulated block to antheridium formation is operative before the loss of sensitivity sets in. It seems predictable, therefore, that, for antheridia to arise in the absence of the antheridial factor, the rate of regenerative development must fall to a still lower value than in the presence of that factor. This consideration may explain the lower proportion of antheridium-forming regenerates in the absence of that factor. It may also account for the delayed appearance of antheridium-bearing wings in the absence of antheridial factor if we consider that wings which first form antheridia in the presence of antheridial factor might undergo regenerative development at too rapid a rate for the formation of these sex organs on medium not supplemented with that factor.

The hypothesis that the excised wings form antheridia without the intervention of the antheridial factor could not remain unchallenged when it was found that the prothalli of *O. sensibilis* produce some antheridial factor even though they fail to form antheridia under the conditions of culture. In the medium, a trace of activity could be first detected at the highest concentration applied (1/2 full strength) 16 days after inoculation. A maximum was reached in approximately 30-day-old cultures when the medium was active to a dilution of 1/10, more rarely 1/30 full strength. The titre remained approximately constant thereafter for a considerable period of time. The 16-day-old prothalli are so small that it was not feasible to obtain a sufficient amount of extract to assay for activity. Extract from 24-day-old gametophytes was active to a dilution

of 1/10, more rarely 1/30 strength. As reported earlier, the extract of older, 45-day-old, prothalli was mostly inactive even at 1/2 full strength[2], but some activity could then be regularly detected in the medium. Perhaps this finding relates to the observation that the basal region had become necrotic in many prothalli of that age.

It should be noted that the last individuals of the gametophyte population became insensitive to the antheridial factor 2–3 days before a trace of antheridium-inducing activity could first be detected in the medium. The results thus indicate that *O. sensibilis* fails to form antheridia under the prevailing conditions of culture because the antheridial factor does not become available until all prothalli have become insensitive to it.

The possibility should be weighed that the wings excised from the 16-day-old prothalli give rise to antheridia in response to the small amount of antheridial factor which they probably contain upon excision. Various experiments indicated, however, that the wings do not elaborate the active substance and that the small amount that may be present on excision would become equilibrated with the medium to an ineffective level before sensitivity to the antheridial factor is restored. Even though these results are consistent with the hypothesis that the excised wings give rise to antheridia without the intervention of the antheridial factor, they cannot be considered conclusive. For this reason no attempt is made to describe the experiments in detail.

It should be possible, however, to obtain more conclusive information with young (still sensitive) prothalli which, according to the available criteria, do not yet elaborate the antheridial factor. Attempts to excise non-meristematic regions from such tiny prothalli proved unsuccessful because most or all of the excised cells died. An alternative approach was therefore chosen.

It was demonstrated many years ago[9,10] that plasmolysis of fern prothalli leads to regenerative cell division and the formation of regenerative outgrowths. Plasmolysis is considered to break the cytoplasmic connexions between neighbouring cells. The authors of these papers concluded that the observed regenerative activity resulted from the disruption of cytoplasmic continuity and the ensuing breakdown in correlative interaction between the meristem and the peripheral areas of the gametophyte.

If the postulated block to antheridium formation actually exists as a function of the meristematic region, then the severance of the cytoplasmic connexions might lead to a decay of the postulated block to antheridium formation and, as a consequence, to the formation of antheridia on medium not supplemented with antheridial factor (that is, in the context of the hypothesis, without the intervention of that factor).

Prothalli on about 1½-mm. thick agar slivers were removed from 6-day-old cultures with a spatula and transferred to 30 ml. of the plasmolytic agent in a Petri dish. The agar slivers which were about 3/4 cm.² in surface area were submerged by applying gentle pressure with the flat surface of the spatula, thus ensuring simultaneous onset of plasmolysis in all prothalli. Following an exposure of 35 min. to the plasmolytic agent, the prothalli, on their agar supports, were transferred to 30 ml. of liquid medium in a Petri dish, where they remained for 35 min. The deplasmolysed prothalli were then returned to agar medium, two agar slivers with prothalli per 50-ml. flask. Sucrose, calcium chloride and mannite were used as the plasmolytic agents.

The temporarily plasmolysed prothalli gave rise to antheridia. Each of the three compounds elicited an antheridial response, even at concentrations that brought about only slight plasmolysis (0·4 *M* sucrose or mannite; 0·15 *M* calcium chloride). The prothalli failed to form antheridia when they were treated with non-plasmolytic concentrations of the three substances (0·3 *M* sucrose or mannite; 0·1 *M* calcium chloride).

The demonstration that only plasmolytically active concentrations are effective supports the assumption that the observed antheridia arise as a function of plasmolysis. This postulate is further strengthened by the finding that the spectrum of effective compounds comprises such chemically diverse compounds as an inorganic salt, a metabolically active organic compound (sucrose) and an organic compound which in all likelihood is metabolically inert (mannite). In turn, it is likely, but difficult to demonstrate conclusively, that plasmolysis is effective because of the ensuing disruption of cytoplasmic continuity.

In a few of the prothalli, antheridium initials could first be seen three days after the 6-day-old individuals were plasmolysed (45 min., 0·6 *M* mannite). (An antheridium was considered to be initiated in the context of this investigation when it appeared as the characteristic semi-circular outgrowth on the initiating vegetative cell.) In non-plasmolysed prothalli the first appearance of antheridial initials followed exposure to antheridial factor within 2½ days in both 4- and 6-day-old prothalli and within a wide range of concentrations (1/10, 1/70 and 1/500 full-strength *Pteridium* medium that was active to a dilution of 1 : 6,000). It is possible, however, that slight differences will be found if the interval of observation used (1/2 day) is shortened. All prothalli ultimately formed antheridia at the above concentrations, while only one in about four responded if the concentration was further lowered to 1/2,000 full-strength *Pteridium* medium. At this limiting concentration, an initial was occasionally found again 2½ days after the antheridial factor was supplied if a large enough sample of prothalli were examined. In other instances three days elapsed at this concentration until antheridium initials could first be seen on a few individuals of the gametophyte population.

If the prothalli subjected to plasmolysis at the 6-day stage were provided with antheridial factor (1/100 full-strength *Pteridium* medium) immediately following deplasmolysis, then the lag period appeared to be intermediate between that encountered with plasmolysed prothalli not exposed to antheridial factor and that observed in non-plasmolysed prothalli exposed to the active substance, that is, about 2¾ days elapsed between deplasmolysis and the appearance of the first antheridium initials.

The above results show that the temporary plasmolysis of 6-day-old *Onoclea* prothalli leads to the first appearance of antheridium initials nine days after inoculation. These initials cannot be accounted for in terms of the antheridial factor unless the assumption is made that the factor is present in the 6½-day-old prothalli (nine days minus the interval of somewhat more than 2½ days

between the exposure of the plasmolysed prothalli to antheridial factor and the first appearance of antheridium initials).

If the antheridial factor were available to 6½-day-old prothalli in the normal sequence of events, then at least some of the individuals in a population of unplasmolysed gametophytes should give rise to antheridia because all are then sensitive to it (with the spore sample used in these experiments, the first individuals of the gametophyte population became insensitive eight days following inoculation). As repeatedly stressed, however, non-plasmolysed *Onoclea* gametophytes fail to form antheridia at any stage of development under the prevailing conditions of culture. The validity of this argument is further strengthened by the observation that plasmolysis of 5-day-old and 4-day-old prothalli also led to the first appearance of antheridium initials within three days. So far as I am aware, this is the earliest reported onset of antheridium formation among homosporous ferns without an extraneous supply of antheridial factor.

Although these results are consistent with the proposed hypothesis, the alternative possibility should also be considered that plasmolysis hastens the onset of antheridial factor synthesis. An attempt was therefore made to assay for the presence of antheridium-inducing activity. Unfortunately, it was not feasible to obtain a sufficient amount of extract from the tiny antheridium-forming individuals to assay for the presence of such activity in the prothalli. It was observed, however, that young (non-plasmolysed) *Onoclea* prothalli failed to form antheridia if they were inoculated among the temporarily plasmolysed, antheridium-forming prothalli of this same species. In contrast, young (non-plasmolysed) *Onoclea* prothalli did form antheridia if they were inoculated among antheridium-bearing prothalli of the six polypodiaceous fern species tested that formed antheridia spontaneously under the prevailing conditions of culture. All these species secrete the active substance into the medium. In the most closely investigated species, *P. aquilinum*, it was demonstrated that the individual prothallus becomes insensitive to the antheridial factor before it begins to elaborate it at an effective concentration[6]. Accordingly, the antheridia arise in response to antheridial factor in the medium (secreted there by more rapidly growing individuals of the gametophyte population[6]).

These results appear to favour the hypothesis that the temporarily plasmolysed prothalli form antheridia without the intervention of the antheridial factor, due to the decay of the postulated block to antheridium formation. Accordingly, they support the proposed hypothesis that the antheridial factor acts by overcoming a block to antheridium formation that prevents the realization of the genetic potentiality for antheridium formation. Attempts are, nevertheless, being made to design experiments that will permit an unequivocal decision between the two alternative interpretations of the results.

It is hoped that these investigations will contribute toward the solution of the problem as to how genetic potentialities for developmental change are realized at characteristic stages of development and how their realization is, at earlier stages, suppressed.

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SITES YIELDING HOMINID REMAINS IN BED I OLDUVAI GORGE

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TOGETHER with Prof. C. Arambourg and Prof. Raymond Dart, I was recently invited by Dr. L. S. B. Leakey to examine the excavations that he and Mrs. Leakey are directing in Bed I at the Olduvai Gorge, Tanganyika.

Bed I consists mainly of volcanic tuffs in the eastern part of the Gorge, but an increasing amount of clay and corresponding reduction in tuffs is observed as one goes westward, so that the westernmost exposures of this Bed consist almost entirely of clays. The tuffs are now all considered to have been laid down under water whereas the bentonitic clay layers with which they are interrelated represent still-water lake deposits. While it was thought by Reck that the coarser beds to the east accumulated fairly rapidly, the clays are considered to have formed only very slowly and in deep water. The edge of the lake shelved gradually, so that periodic fluctuation in water-level would have exposed an appreciable area of the lake margins for temporary settlement. Dr. Leakey states that the fauna includes forms related to the okapi and sitatunga, which indicate a climate wetter than that found at Olduvai to-day and sufficient to maintain swamp and rain-forest. The latter may have been relict patches of an earlier extension, since forms such as lion, cheetah, hyena, horse, hartebeeste and gazelle, which are also represented in the Bed I fauna, usually prefer savannah or grassland country.

We spent up to two days examining the horizons in which the excavations are being conducted, and I had one day in the Coryndon Museum, Nairobi, working on representative collections from the excavations. Besides the main site *FLK*.I from which the skull of *Zinjanthropus boisei* came, we examined three other excavations in Bed I (*FLK.NN* ; *FLK.N*I and *MK*.) as well as four in Bed II (*FLK.N*II ; *FLK*.II ; *BK*.II and *HWK*.II).

At *FLK*.I the *Zinjanthropus* horizon lay on and in the top of 1–2 in. of a thin, bentonitic clay layer, and some 70 ft. × 30 ft. of this had been exposed at the time of our visit. Although most of the floor had been lifted prior to our arrival, a section some 2 ft. × 15 ft. remained, and from this and the horizontal grid plot, the nature of the floor and the position of every find could be clearly seen. The nature of the scatter pattern on these excavated floors is always the same, and the faunal and cultural material lies on the surface of the clay or in the topmost few inches. Similar bone concentrations are absent from the immediately over- and under-lying beds (yellowish tuffs).

The floors, or temporary land surfaces, are usually flat or very gently undulating, and represent exposed and dried mud-flats which became available for temporary settlement by the recession of the lake waters.

Although the usual geological signs of seasonal fluctuation of water-level are absent from the sites, yet it is hard to see how the bone on the living floors could have remained in the unweathered state in which it is found unless the surface had been fairly quickly covered again by the lake waters or unless the mineralization process had begun almost immediately. Bone lying to-day on the surface in the tropics splits up and disintegrates rapidly, and often exposure for only one or two seasons is necessary for chemical and biological agents to destroy it. I have observed that in tropical climates with alternating wet and dry seasons and high diurnal temperatures, the higher the rainfall the quicker bone is destroyed. If, however, the climate when these land surfaces were exposed had been more temperate, with more evenly distributed rainfall and lower temperatures, it is probable that the speed with which bone would be destroyed would be considerably slowed down. I observed on these floors only a few bone fragments which showed evidence of natural weathering, so that unless some such climatic adjustment is postulated it is difficult to understand how the living sites on the surface of the clays could have been exposed for any long period of time before they were again covered. Such exposure and burial must be related to temporary periodic fluctuations in the water-level, perhaps even to seasonal fluctuation, as can be seen occurring to-day around the edge of Lake Manyara, for example.

The faunal and cultural remains occur in a similar manner on each of the three areas where the old land surfaces have been excavated; that is to say, they are scattered in varying concentration over the surface. They consist of broken and sometimes complete bones as well as natural and artificially fractured stone, both quartz and lava. On *FLK*.I, the horizontal plot shows clearly a roughly circular concentration of smaller bone fragments, many small flakes and flake fragments and other worked pieces of quartz and lava over a 15-sq. ft. area. Outside this, the bone and stone occur much more sparsely, except for a rough arc of larger bone fragments and stones a few feet distant on the side from the main concentration.

At *FLK.NN*, artificially fractured and all other stone is very rare, and on some of the faunal remains the marks of teeth, radiating fractures and possible gnawing of the articular ends of long bones suggest that carnivores may have been responsible for part of this accumulation. There is no obvious evidence of carnivore (lion, leopard or hyena) activity at *FLK*.I or *FLK.NI*, however. On these sites the bone fragments consist usually of small sections, splinters and articular ends of long bones and broken mandibles, mainly of pig, antelope and horse, with some reptile and bird bone. Complete animals are never found, so that such parts as are preserved may have been obtained mainly by scavenging.

The number of animals represented on the floors was never large, but it was sufficient to suggest that the remains were carried in rather than that the floor represents a kill site. The shafts of many of the long bones have clearly been fractured to extract the marrow, and the articular ends lie discarded nearby. Sometimes shaft fragments show comminuted fracture on the interior surface, such as experiment shows results from smashing and crushing with a rounded, blunt tool.

Both the natural and artificially fractured lumps of lava and quartz, rarely more than the size of the fist, must have been intentionally carried to the positions where they were found. Every indication is that natural wash must be excluded, and there is never any sand, grit or fine gravel associated with the material on the floors—only the stones and bones lying on the clay. Moreover, as the fractures of nearly all the bones, as of the worked stone, are quite fresh, these floors must, as already stated, have been covered rapidly after their occupation.

The natural stones are likely to have been tools or potential tools just as much as the fractured ones. These last consist of gradations of 'bashing stones', from natural lumps with one or two flakes removed to full polyhedral forms; there are many flakes struck unintentionally from these. Other specimens have been intentionally flaked, usually bilaterally, to form chopping tools, and the flakes struck from these are also likely to have been used, though, unlike those in Bed II, they show no evidence of intentional retouch or unquestionable utilization. The number and standardization of specimens clearly indicate a regular pattern of intentional manufacture. A statistical comparison of the choppers and polyhedral stones and cores with the flakes and flake fragments from these floors will be of considerable interest and may show whether any of these tools might have been made elsewhere and afterwards carried to the site.

The two horizons in Bed I (*FLK*.I and *FLK.NI*) showed every indication that they were temporary living places of the hominid which made the Oldowan implements and broke up the bones lying on these floors. The evidence we saw excludes any other interpretation. Hominid remains have now been found in intimate association at three horizons in Bed I (*FLK*.I; *FLK.NNI* and *MK*.) and, should no other more advanced form of man be found in this bed, there would be strong reason to accept *Zinjanthropus* as the toolmaker.

I wish to thank Dr. Leakey for making this visit possible and for providing opportunities for discussion with two eminent colleagues. There can be no doubt that these excavations, which have already uncovered so much—from the remains of a complete *Deinotherium*, most of the bones of which had been reduced to a pink powder, to the poison fang of a puff adder—have every possibility of finding the remains of any other hominid, should such have existed contemporaneously with *Zinjanthropus*.

LETTERS TO THE EDITORS

GEOPHYSICS

Southern Hemisphere Fall-out and the Meridional Circulation

THE interpretation of the role of the stratosphere in determining the global fall-out pattern of radioactive debris has recently moved towards a compromise of a number of models.

Libby[1] suggests that a plausible explanation of measurements of the stratospheric burden and of surface fall-out can be advanced in terms of: (*a*) Martell's theory[2] of an 8–12 month residence time for polar latitudes and one of several years for equatorial debris; (*b*) the Machta model[3] in which the concentration of fall-out in middle latitudes is associated with a meridional circulation in the lower stratosphere[4].

Stewart[5] first suggested that the spring increase in fall-out was a result of such a mean circulation. Libby notes that this concept of stratospheric air rising at the equator, and falling elsewhere, particularly in polar regions, is consistent with an early fall-out for polar injections.

In a previous report describing measurements of total β-activity in rainwater at Melbourne[6], quantitative evidence was advanced that a mean poleward circulation in the lower stratosphere of about 1 m./sec. was largely responsible for the latitudinal spread of debris in the southern hemisphere. The existence of such a circulation is favoured on purely meteorological grounds[7,8].

Further measurements of fall-out presented here give additional support to the idea that the meridional circulation plays a significant part in determining the global fall-out pattern. The results are given in Fig. 1 in the customary units of μμc./l. (The sampling area used was $2{\cdot}2 \times 10^3$ cm.^{2}.) These are also presented in arbitrary units of quantity of material by correcting for decay following Hunter and Bøllou[9], on the assumption that half the material is due to the 1958 'Hardtack' tests, and that half originated in 1955. (The latter date represents a compromise between the 1954 'Castle' and 1956 'Red-Wing' tests.) The most drastic revision of this assumption, which is based on Libby's injection results and a two-year stratospheric half-residence time, would affect the shape of the corrected curve by a negligible amount.

The most striking feature of Fig. 1 is the pronounced seasonal variation, with peaks in late 1959 and 1960 occurring roughly during the spring in the southern hemisphere. The peak in early 1959 can be associated with the initial arrival of debris from the 1958 'Hardtack' series. This seasonal variation must be regarded as a meteorological effect since no high-yield tests have been conducted in the southern hemisphere at any time. Stewart's view of an enhanced meridional circulation during the winter is therefore a most attractive explanation.

The total β-activity of fall-out during 1959 measured at Melbourne in the present investigation was 13 mc./km.^{2}, and with the above assumption regarding the time of origin of the debris, a strontium-90 fall-out of 1 mc./km.^{2} can be estimated. This agrees satisfactorily with the value of ~ 1·3 mc./km.^{2} reported by the H.A.S.L. project for these latitudes[10]. During the same period, stratospheric soundings[11] indicated that the average strontium-90 concentration at 38° S. and 200 mb. was approximately 5 d.p.m./1,000 S.C.F. (that is, 2×10^{-13} c./m.^{3}). If mean vertical motion is solely responsible for transfer across the tropopause, an average vertical velocity of 200 m./day at 200 mb. can be inferred. Somewhat smaller values would be obtained at greater heights.

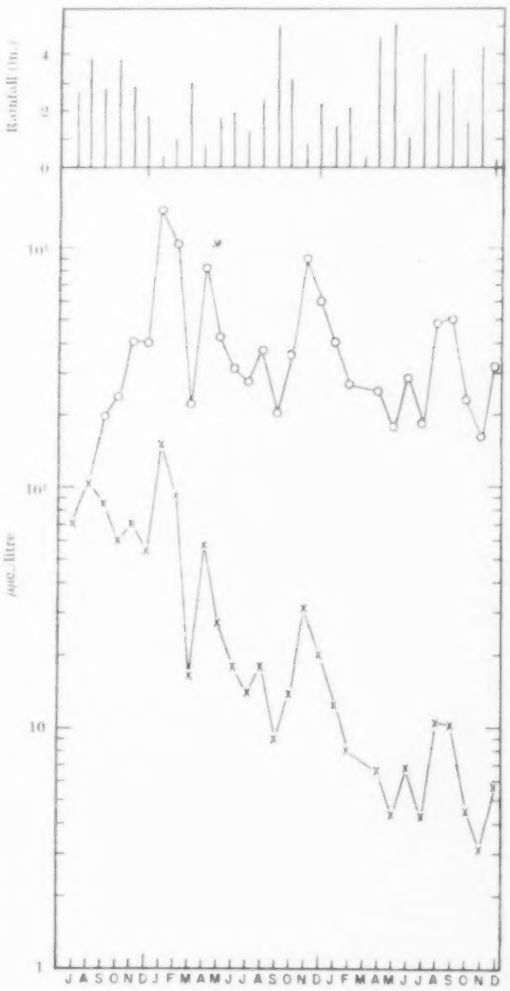

Fig. 1. Monthly fall-out data at Melbourne, Australia. ×, total β-activity; ○, corrected for decay

This is an obvious over-simplification, and estimates of mean vertical velocities of 50 m./day and 120 m./day by Brewer[4] and Priestley[7], respectively, suggest that roughly half the downward movement of debris can be attributed to mean motion and half to eddy transfer.

At our present state of knowledge of stratospheric meteorology there is considerable room for conjecture; but it seems clear that, in interpreting global fall-out, the role of the mean meridional circulation cannot be ignored.

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RADIOPHYSICS

Ionospheric Scattering of Satellite Transmissions

Radio waves from satellites may fade in both regular and random fashion when received with a linearly polarized aerial. Fading due to Faraday rotation or satellite rotation is an example of the former type. Random fades, up to several per second, are sometimes observed, and these have been attributed to scattering from the same kind of ionospheric irregularities as produce radio star scintillation. This fading is more rapid for satellites than for radio stars since it depends on satellite velocity rather than ionospheric drift velocity. Henceforth we shall be concerned only with the randomly fading component.

The 40 Mc./s. transmission from *Sputnik I* has been recorded at Cambridge by Kent[1]. It was observed to fade rapidly at night, but only when the satellite was to the north of Cambridge. The transition to or from this rapidly fading condition was quite abrupt. Kent has concluded that the irregularities which cause the fading are present only to the north of Cambridge; but Mawdsley[2] has suggested that the effect is a natural outcome of the anisotropic nature of irregularities which appear to be aligned with the Earth's magnetic field. Thus, generally speaking, strong forward scattering should be observed only when the satellite is poleward of the observer.

We have recorded the 19·990 Mc./s. transmission of *Explorer VII* at Wellington, New Zealand. Observations commenced recently when details of this satellite came to our notice through the *International Geophysical Year Bulletin*, No. 29, of the U.S. National Academy of Sciences. Table 1 lists the passes during which recordings were made before the orbit moved completely into daylight conditions over Wellington. Scintillations were observed only when the satellite was to the south at night. The transition was abrupt.

Table 1

Date	Local time of pass (approx.)	Remarks
3.6.60	2052–2100	Scintillations when satellite to south
..	2235–2245	.. ..
4.6.60	2027–2036	.. ..
7.6.60	1357–1404	No scintillations
..	1541–1550	.. ..
..	1728–1735	.. ..
..	1913–1925	.. ..
..	2100–2110	Scintillations when satellite to south

A search of the literature has since brought to light several instances of similar behaviour. They are as follows:

(1) Kraus and Albus[3] made signal strength and Doppler frequency shift measurements of the 20·005 Mc./s. transmission from *Sputnik I* at Columbus, Ohio. Scintillations were recorded as the satellite rose in the north, ceased abruptly as the satellite approached the station, and were absent for the rest of the pass. This behaviour was not apparent on south-to-north passes. It was suggested that an ion cone might precede the satellite, forming an unstable medium for waves passing through it. More recently, Hamé and Kennaugh[4] have extended these observations to the 20·005 Mc./s. transmission from *Sputnik III*. They find that scintillation occurs only when the satellite is north of Columbus irrespective of the direction of pass. They have suggested an explanation in terms of changes in magneto-ionic propagation as the Earth's magnetic field varies according to the position of the satellite. It is difficult, however, to see how to explain a change from regular to random fading in this way.

(2) Recordings of signal strength, Doppler frequency shift, and bearing angle of the 20·005 Mc./s. transmission from *Sputnik I* have been made at Komuro, Japan, by Miya *et al.*[5]. Referring to Fig. 2 of their paper, a sudden change in fading pattern was recorded when the satellite was near the station. South of this point the random fading is small compared with Faraday fading. The more intense rapid fluctuation when the satellite is in the north could perhaps be due to scintillation if the recording system had the characteristic of a low-pass filter. Miya *et al.* ascribe the transition as one between line of sight propagation and regular ionospheric propagation associated with ground scattering. However, the transition of Fig. 2 of their paper occurs when the satellite is quite close to the station. Fig. 6 shows fluctuations in bearing angle when the satellite is 'in view' north of the station. The fluctuations disappear as the satellite moves to the south.

(3) Fluctuations in Doppler frequency change at Portsdown, England, of the 20·005 Mc./s. transmission from *Sputnik III* have been noted by Kitchen and Joy[6]. Fig. 3 of their communication shows an example of this behaviour, which is apparent only to one side of the station. The fluctuations have been attributed by these workers to small-scale *F* region irregularities.

(4) Sudden fluctuations in the signal strength at Kiruna, Sweden, of the 20·005 Mc./s. transmission from *Sputnik III* have been reported by Liszka[7]. Fig. 1 of his communication suggests that the fluctuations may be asymmetric with respect to the observing station. Because these fluctuations occur at similar positions for successive orbital revolutions, Liszka has suggested that long-lived heavily ionized tracks are produced by the passage of the satellite through the

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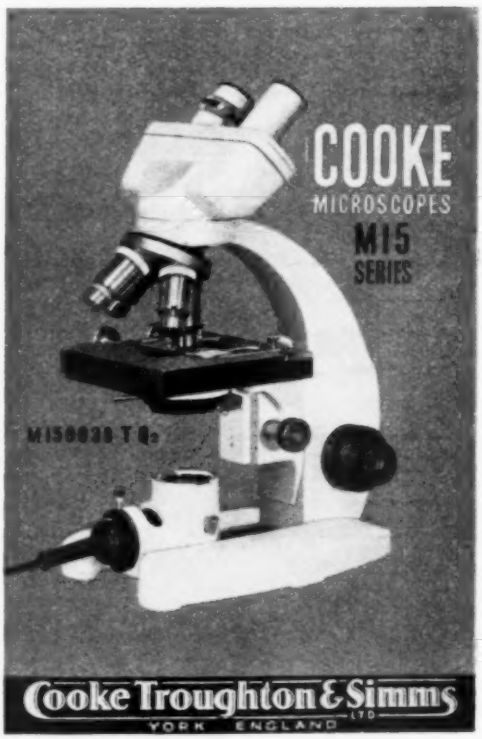

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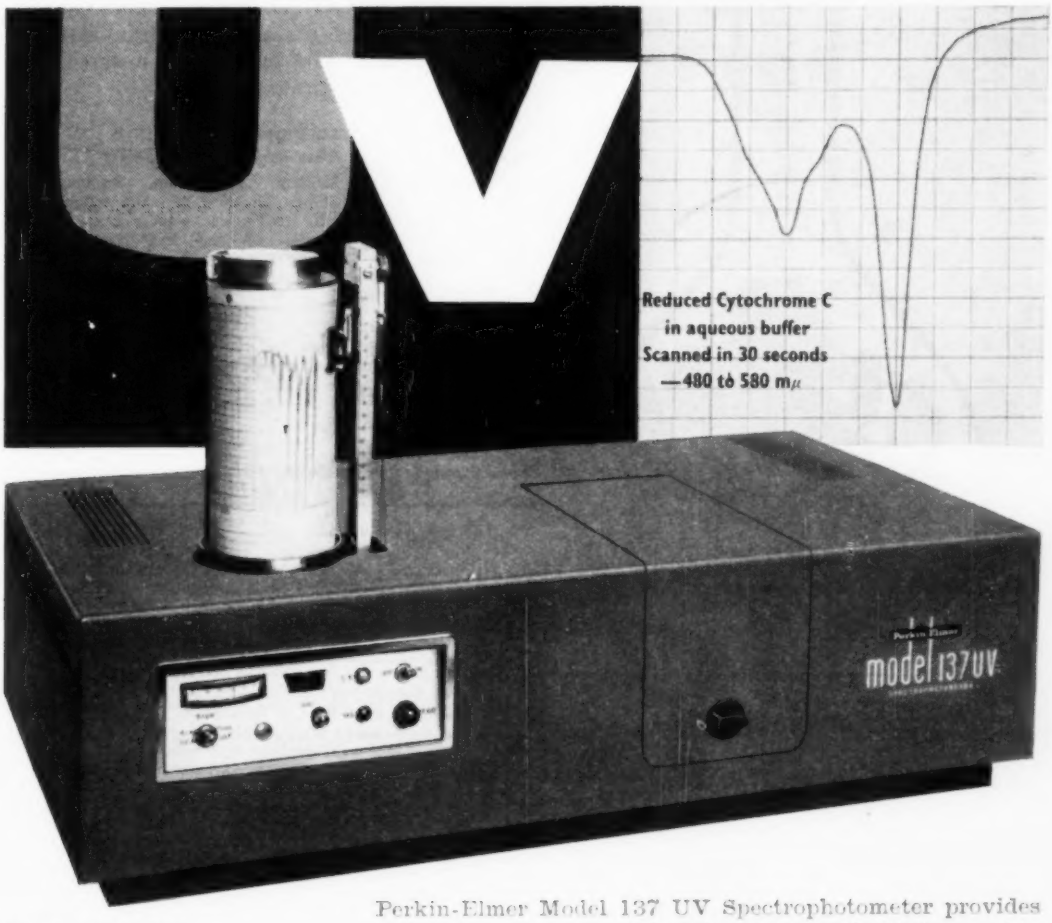

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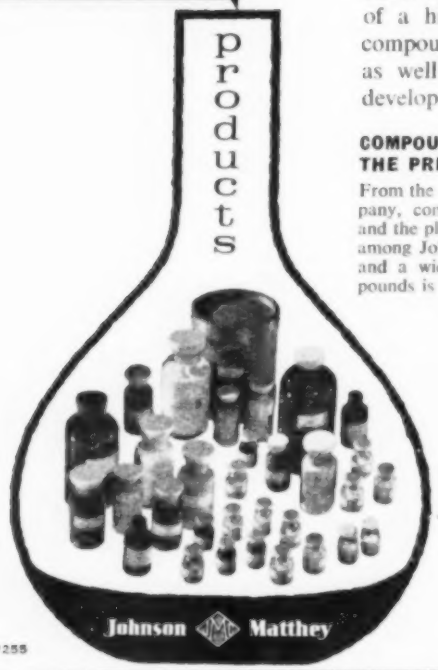

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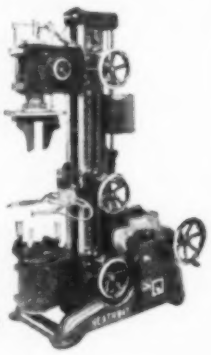

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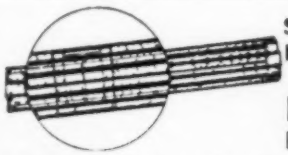

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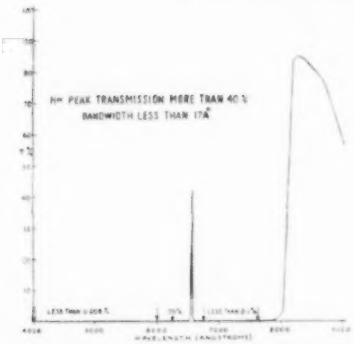

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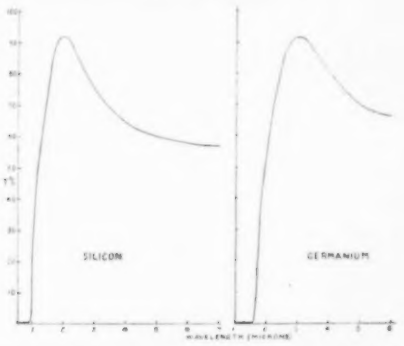

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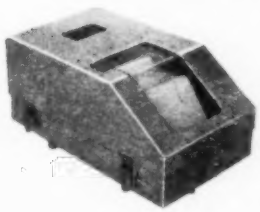

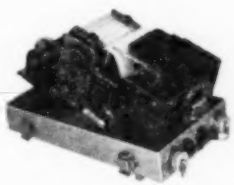

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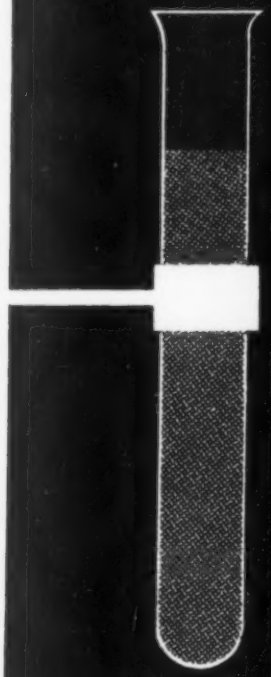

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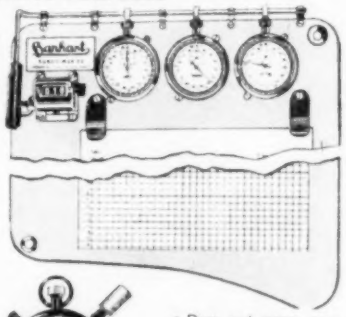

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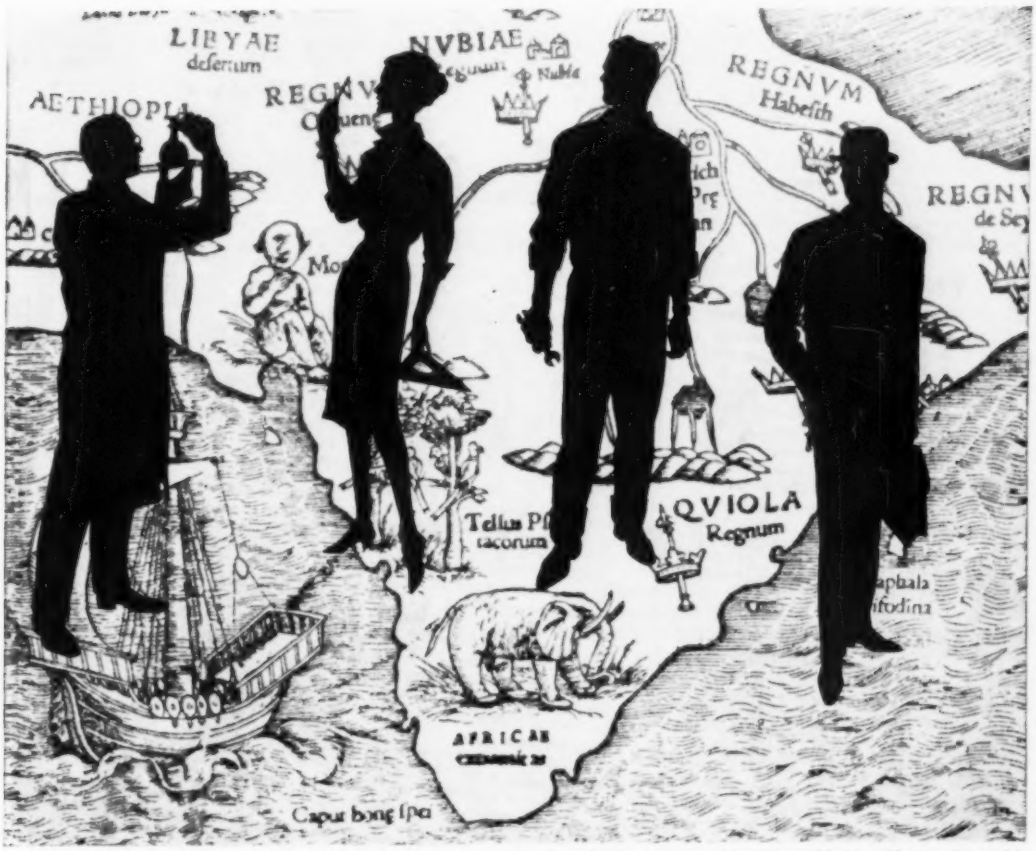

A woodcut map of Africa (Sebastian Munster, 1540). Reproduced by courtesy of the National Maritime Museum, Greenwich.

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The place of the Particle Accelerator in Basic Research

Particle Accelerators for Nuclear Physics Teaching - IV

Laboratory demonstrations of nuclear phenomena are invaluable in illustrating the problems that will be encountered by the student in nuclear physics research. They are a vital adjunct to classroom instruction in theoretical and experimental nuclear physics. The experiments themselves should illustrate the techniques commonly used for particle detection, as well as problems that will be encountered in vacuum systems, high-voltage breakdown, and general electronic and nucleonic instrumentation.

A most fruitful method for nuclear investigation involves high-energy bombardment of the target nuclei. A number of charged-particle accelerators are available for this type of work, one of the most useful and versatile of these being the Van de Graaff. High Voltage Engineering Van de Graaff equipment can produce homogenous beams of protons and deuterons with continuously variable energy. Accelerators are available with maximum energies of 0.25, 1.0, 2.0, and 3.0 Mev. These allow many heavy-particle reactions to be demonstrated, as well as several photonuclear reactions above 1.66 Mev.

Scattering Experiments

Proton-proton scattering experiments are readily carried out with hydrogenous targets, and can be used to demonstrate isotropic scattering in the center-of-mass system characteristic of

Energy-level diagram for Be^8 from (2).

s-wave interactions. The heavier nuclei in the target material will produce a different energy-angular relationship and thus demonstrate the effects of high-Z materials. Analysis of the data can illustrate the difference between the high- and low-Z materials, and show the departure from pure Rutherford scattering with low-Z targets.[3]

Nuclear Reactions

Some typical reactions can be shown using a Li^7 target. The first two excited levels of the compound nucleus in the reaction Li^7 (p,γ) Be^8 can be determined by measuring the gamma rays emitted at the 0.441 key resonance. Measurement of the energies of the alpha rays resulting from the disintegration of the Be^8 nucleus can be used to determine the angular momentum and parity of the excited nuclear levels. The energy-level diagram shows these levels[2], the cross-section for the various reactions is sketched at the right hand side. Inelastic proton scattering of the incident protons can also be demonstrated and shows resonances at 0.8 and 1.04 Mev[3].

Neutron Production

Neutron production is also possible with suitable particle target combinations. The D-D reaction will produce neutrons with energies of the order of 2 Mev. The D-T reaction will produce neutrons with energies of the order of 14 Mev[4]. These fast neutrons can be used to demonstrate neutron-nuclear phenomena such as moderation, inelastic scattering, and capture with resultant radioactive decay.

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Typical experiments such as those described can be applied to show the student how to analyze experimental data, and how to use different types of particle and electromagnetic radiation detectors. They also bring to the attention of the student some of the problems which are still unsolved in the theory of the nucleus.

The advanced nature of the Van de Graaff accelerator design, suitable for teaching at the student level, also permits original research programs to increase man's understanding of nuclear phenomena.

Write to HVEC for a set of typical experiments which can be performed with pulsed or continuous neutron sources.

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atmosphere. This repetitive spatial occurrence is, however, a natural feature of scattering sensitive to aspect from irregularities aligned with the Earth's magnetic field. Although *Sputnik III* may not have passed north of Kiruna (geographically) it is to be noted that, because the magnetic field lines there are nearly vertical, energy may still be scattered from a satellite in the south to an observer in the north.

(5) More recently, Yeh and Swenson[8] have undertaken a detailed analysis of scintillations, observed chiefly on the 20·005 Mc./s. transmission of *Sputnik III*, at Urbana, Illinois. Night scintillation is associated with *F* region and is observed only when the satellite is in the north.

In view of the possible association with radiation belts[9] it would be useful to have scintillation observations over an extended period covering a wide range of latitudes. Few radio stars are suited to this purpose, particularly for the southern hemisphere. Thus, although it may be desirable from some points of view to interrogate the majority of future satellites, there is a strong case for providing a few which transmit continuously at a frequency between about 20 and 40 Mc./s. for some time to come.

In conclusion it appears likely that the night-time scintillation of satellite transmissions demonstrates the ability of field-aligned irregularities to scatter metre wave-length radio waves in a manner highly sensitive to aspect. This is not to be expected of such gross features as are deduced from radio star scintillation or from Kent's observations. Some fine structure must be sought, such as might arise when aggregates of charged particles spiral into the atmosphere along magnetic field lines and create ionized tracks.

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ASTROPHYSICS

Galactic Motions in a Large-Scale Magnetic Field

Recent observations on spiral galaxies have shown that their interstellar material cannot be in purely rotational motion. The evidence points to a circulation of interstellar gas between the galactic plane and the galactic halo.

It has been shown for several galaxies[1], including our own[2], that the observed differential rotations will, within less than 10^9 years, transform an initially structureless interstellar cloud into a spiral arm having a pitch like that of observed arms. Since spiral structure presumably persists for longer than 10^8 years, it was suggested that arms may somehow be preserved to 'look young'[2]. However, I[3] have shown that one likely mechanism, magnetic fields embedded in the arms, cannot achieve this; on the contrary, these fields disperse an arm within 10^8 years by their lateral magnetic pressure and an associated transfer of angular momentum. Other evidence that the arms are actually young comes from the observations of Rougoor and Oort[4] that the '3-k. parsec arm', an arm of neutral hydrogen about 3 k. parsec distant from the galactic centre, moves radially outwards with a speed of roughly 50 km./sec. Similar motions have been observed by Münch[5] in the galaxy *M*31. According to observations by Pismis[6] and by Kerr[7], even the well-established spiral arms in our galaxy are moving away from the centre with a velocity of roughly 5 km./sec. At this rate no arms of interstellar gas can remain in the galactic plane after 2×10^8 years unless new arms are formed near the centre.

If the 3-k. parsec arm is a continuing or recurrent phenomenon, the galactic centre is an insufficient source of gas[4]. Furthermore, the 3-k. parsec arm demands a source of angular momentum since it participates in the local circular motions and the angular momentum involved in these motions increases outwards[4]. Hoyle and Ireland[8] investigated the effect of interstellar magnetic fields, but they assumed that the angular momentum gained by the 3-k. parsec arm is derived from elsewhere in the galactic plane. This implies that another cloud of gas should approach the centre, which is not observed. We must, therefore, look to the galactic halo as a source of both gas and angular momentum. The drain of gas from the halo near the centre and the radial motion in the plane imply a return of the gas to the halo. As suggested by Hoyle and Ireland[8], this may occur by means of magnetic bubbles rising from inter-arm regions.

Therefore, both observational and theoretical arguments indicate the existence of a large-scale circulation of the interstellar gas and of its angular momentum between the galactic plane and the halo. Such a circulation can be driven only by interstellar magnetic fields. Davis and Biermann[10] have recently discussed possible models of the galactic halo. They suggest that field strengths of 2×10^{-5} gauss in the plane and 6×10^{-6} gauss in the halo and a gas density of 10^{-2} hydrogen atom per cm.^{3} in the halo are compatible with observations and theory. Although a detailed model of the circulation would be very premature (even the very similar problem of the hydromagnetic dynamo has not been solved satisfactorily), some features may be pointed out which may guide further tests on the possibility of the proposed circulation.

First, superposed on any local turbulence there must be magnetic and velocity fields of a much larger-scale size, of the order of several kiloparsecs. Because of the large electrical conductivity the energy involved in these fields will be dissipated only through interaction with the small-scale turbulence. This is probably small, so that the circulation can be maintained over times longer than 10^9 years and thus preserve the spiral structure of the galactic plane.

Second, since the gas density decreases away from the plane much more rapidly than the field strength, the large-scale field in the halo can control the motion of the gas. This may permit the 'unwinding' of the magnetic fields which have been wound up by differential rotation in the plane and have risen into

the halo together with the gas in which they are embedded. The gas being dispersed throughout the halo must stream predominantly along lines of force since the field strength would otherwise decrease proportionally to the gas density. Since the supply of gas and of angular momentum in the halo is comparable to that in the plane, the unwinding of the field and the dispersal of the gas need not occur very rapidly. Probably the field will adjust itself to a rather force-free geometry. But as Schlüter[11] has shown, even a perfectly force-free magnetic field can transport momentum and angular momentum. Hence a circulation of energy and of angular momentum appears possible, with the gas moving radially outwards in the plane, gaining energy and angular momentum from gas moving inwards through the halo.

Finally, I have attempted to make some estimates on the forces acting on the gas at the centre and in the 3-k. parsec arm. For this purpose I assume that the large-scale magnetic field within regions of high gas density is axisymmetric, although no such symmetry is to be expected outside these regions. The assumption is justified primarily by the conclusions which can be drawn from it. Let R and ϑ denote the distance from the centre and the angle in the direction of the galactic rotation. The rate of transfer of angular momentum to a unit mass of gas in the galactic plane at a density ρ is (in c.g.s. and gauss units):

$$\frac{\mathrm{d}}{\mathrm{d}t}(Rv_\vartheta) = \frac{H_R}{4\pi\rho}\frac{\mathrm{d}}{\mathrm{d}R}(RH_\vartheta)$$

On the assumption that the field lies parallel to the trailing arms we find that H_ϑ and H_R have opposite signs. The quantity $|RH_\vartheta|$ must attain a maximum at some $R = R^*$ since it vanishes at the centre and decreases outwards at the edge of the galactic plane[12]. The gas within R^* loses angular momentum and must be moving inwards; the gas outside R^* gains angular momentum and moves outwards. Hence gas must condense on to the galactic plane near R^*. Presumably it moves at different rates on either side of R^*. I conclude that on each side of the galactic plane there must exist two circulations which meet on a surface through R^* but do not interfere with each other. This implies that the magnetic fields are self-contained and angular momentum is conserved in each circulation. The neutral hydrogen within 1 k. parsec from the centre is observed not to expand with the surrounding 3-k. parsec arm[4]. Accordingly, I identify $R^* = 1$ k. parsec and make the following numerical estimates for the outer ($R > 1$ k. parsec) circulation, which involves all the spiral arms: near the Sun, $H_\vartheta = 2 \times 10^{-5}$ gauss; near $R = 4$ k. parsec, $H_\vartheta = 4 \times 10^{-5}$ gauss (negligible transfer of angular momentum outside $R = 4$ k. parsec); and at the 3-k. parsec arm, $H_\vartheta = 7 \times 10^{-5}$ gauss, $H_R = -0{\cdot}25\ H_\vartheta$, $\rho = 0{\cdot}4$ hydrogen atom per cm.^{3}. The resulting transfer of angular momentum permits the 3-k. parsec arm to move radially outwards with a speed of about 50 km./sec. and still to participate in the local circular motions. Thus the assumption of axisymmetry within regions of large gas density results in the explanation of the isolated central region and of the velocity of the 3-k. parsec arm. Furthermore, these estimates imply that gas may rotate more slowly than stars at the same R, since the gradient of the magnetic field causes forces on the gas which partly balance the galactic gravitational attraction.

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Some Solar Lines in the Infra-Red Spectrum observed from a High-Flying Aircraft

In a previous communication[1], it was pointed out that strong absorption by atmospheric constituents obscures large parts of the infra-red spectrum from ground-level observation. However, by working at high altitudes and by using a high-resolution spectrometer, it is possible to observe additional features due to absorption in the solar atmosphere. Among these are two absorption lines due to the electronic transitions in solar hydrogen 3–4 and 4–8, which occur in the great water-vapour band at 1·9μ.

These lines, which have not previously been detected because of obscuration by water-vapour absorption—even at mountain observatories—are clearly observed at 40,000 ft., as shown in Fig. 1. They remain of the same intensity at higher altitudes, thus confirming their solar origin.

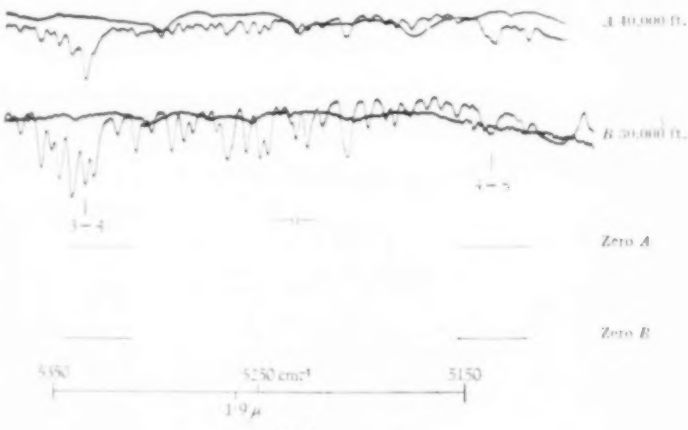

Fig. 1

Another solar line which we have now detected at high altitudes is the 4-6 transition, lying in the 2·6μ water-band. The presence of this line will produce slight corrections to some of the water-vapour concentrations calculated by Houghton and Seeley[2].

Full results of our measurements are being submitted to the Royal Society for publication in the *Philosophical Transactions*.

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PHYSICS

Line-Spread Functions of Photographic Emulsions

The detail-recording ability of a photographic emulsion may be tested by exposing it through a very narrow slit, and, after processing, measuring the variation of density with distance, x, from the centre line of the image. When the scale of density is transformed into a scale of effective intensity of illumination, the result is the line-spread function, $B(x)$.

Traditionally, the 'double-exponential' function[1-3] is taken as a convenient model for the analytical representation of measured results. For the present purpose, this function may be expressed as:

$$B(x) = \pi F \exp(-2\pi F|x|)$$

Its Fourier transform, the sine-wave response function, is:

$$Y(f) = 1/\{1 + (f/F)^2\}$$

where f is the spatial frequency and F is the value of f such that $Y(F) = 0{\cdot}5$. In generalized form, these functions are shown as the dashed curves in Figs. 1 and 2. Some workers, however, have indicated dissatisfaction with this model, referring either to its physically unlikely sharp peak and central discontinuity or to the related slow fall of sine-wave response at the higher frequencies. Various modifications have been proposed, but most involve at least one additional parameter.

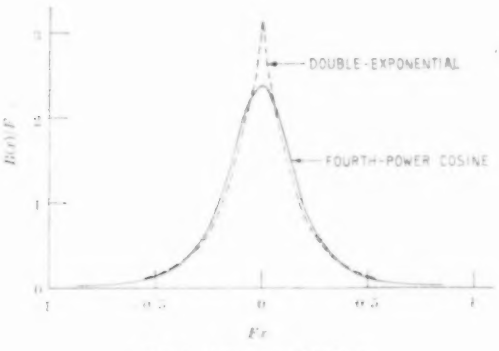

Fig. 1. Line-spread functions

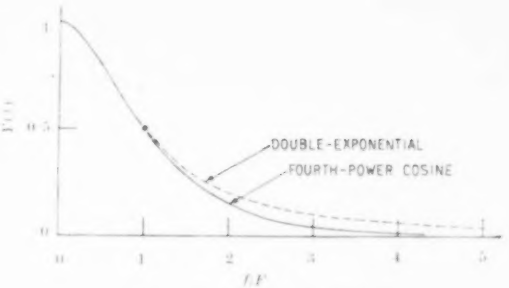

Fig. 2. Sine-wave response functions

In the course of work on television image structure, it has been noticed that the 'fourth-power cosine' function, as it may be termed, offers advantages as a model line-spread function. Expressed in terms of a length parameter, D, the function is:

$$B(x) = 2\cos^4\{\tan^{-1}(x/D)\}/\pi D$$
$$= 2/\pi D\{1 + (x/D)^2\}^2$$

or, in terms of the parameter F already defined:

$$B(x) = 2AF/\pi\{1 + (AFx)^2\}^2$$

where $A = 3{\cdot}7437$. The corresponding sine-wave response function is:

$$Y(f) = (1 + 2\pi Df)\exp(-2\pi Df)$$
$$= (1 + 2\pi f/AF)\exp(-2\pi f/AF)$$

Generalized in terms of F, these functions are shown as the full-line curves of Figs. 1 and 2.

Comparing the curves in Fig. 1, it will be seen that the fourth-power cosine function is closely similar to the other in the region of the 'skirts', but it has the desirable property of being less-sharply peaked and there is no central discontinuity. The related features in Fig. 2 are the similarity at the lower frequencies and the more-rapid fall at the higher frequencies.

For describing line-spread functions in general, the half-intensity width, W, is often a useful parameter. In symmetrical functions, W is defined by $B(W/2) = 0{\cdot}5$ whence, for the fourth-power cosine function:

$$W = 0{\cdot}3438/F = 1{\cdot}2872D$$

Taking a medium-speed panchromatic film as an example, it is believed that W might typically be 15μ, whence $F = 23$ lines/mm. and $D = 12\mu$. A fair approximation to the subjective resolving power determined with a high-contrast target is often given by 1/W; this is 67 lines/mm. in the example.

If the proposed function proves in practice to be a good model, its relation with the well-known $\cos^4\theta$ law of off-axis illumination in an optical imaging system will be of interest. However, whether or not the θ of that law can be identified with the $\tan^{-1}(x/D)$ of the expression for $B(x)$ first given, it may possibly be significant that the distance D appears to be about equal to the emulsion thickness.

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Detection of Free Charges from Motor-Car Exhaust Gases

THE production of charged entities during combustion is well known[1], and some of these entities have proved to be gaseous ions of low molecular weight containing carbon and hydrogen or oxygen and hydrogen[2]. It is known that ionization takes place in explosion motors and it is used, for example, to detect ignition induced by deposits[3]. Jet aeroplanes are reported to become charged electrically[4]. Part of the charging current (about 500 μamp.) might be due to the preponderance of free charges of a certain sign in the exhaust gases.

In an investigation of the role of unipolar radical ions in radiation chemistry and their radiomimetic properties and possible role in the initiation of lung cancer[5], I have done some preliminary work on the presence of free charges in motor-car exhaust gases and from other sources. The apparatus consisted of a charge collection chamber with a geometry rather similar to that used by Siksna[6] (see Fig. 1). The unit is easily portable (the high-tension device is made with transistors). Careful tests have been done to ensure that creep currents are negligible even under very moist conditions. To this end, the 'Teflon' insulator is heated electrically. The output of the instrument is proportional to the concentration of charge in the gas. In more stationary cases, I have used a large parallel-plate condenser[7] (plate separation distance, 100 mm.; size 300 mm. × 300 mm.) to measure the total current that can be collected, by applying a field-strength of 300 V./cm. This unit measures total rate of production of charge rather than concentration of charge.

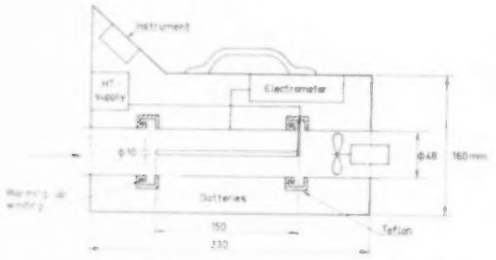

Fig. 1. Portable charge collection apparatus. Air velocity 1 m./sec. Transistorized high-tension variable, 700–1,200 plus or minus. Charge collected at outer electrode is amplified by a conventional electrometer tube circuit. The insulator is heated by mercury batteries. All dimensions are in millimetres

Virtually every car tested (about forty so far) exhibited charge production. On starting the engine, the production is low but increases to high steady states (often $\sim 10^7$ charges/cm.^{2} at full throttle. The total current collected varies from car to car. In the worst case, a current of 100 μamp. was detected, or more than 10^{14} charges/sec. The positive and the negative parts were nearly equal. In this vehicle, the silencer was in bad condition. Small motors, for example, from 'mopeds', were found to yield rather low currents, namely, about 10^{-9} amp., or slightly more than a cigarette[8]. The charges are confined to the exhaust gas cloud. The concentration drops steadily with distance from the exhaust tube. Nevertheless, I have detected charge concentrations on the pavements of streets with heavy traffic and in the back-seats of cars driving behind Diesel trucks. Starting a car in a garage fills the space rapidly, with a charge concentration which, however, drops in some tens of seconds if the car leaves the garage. The charge monitor is provided with variable collector voltage so that some information on the mobility spectra can be obtained. However, the conditions have not been steady enough to facilitate observations of this kind.

The level of the concentration is roughly the maximum that could be expected from a gas-ion recombination[8], but we are not justified at present in making any exact statements on the nature of the charges detected. There are strong arguments[2] for believing that molecular gaseous ions are produced in explosion motors. The fate of these ions will, however, be dependent on the properties of the exhaust tube, the presence of filters (it is known that wool eliminates most of the ions[9]), the humidity and presence of water or oil droplets, dust, etc. The latter may sorb a large part of the original ions. Further work will have to be done to explore the nature of the charges at different times. It is likely that free radicals can be detected by condensing rapidly the exhaust gases from explosion motors, as is the case for cigarettes[10]. In many other instances, apart from explosion motor exhaust gases, charges have been detected, for example, in gas and electrical welding, smoking of cigarettes and cigars[5], household cooking gas and flames and glowing bodies (such as bread-toasters).

Further study of the nature of these charges would seem to link radiation chemistry and radiation biology with the field of air pollution and public health in an interesting way. If it turns out that the charges represent radiomimetic entities, much can be done to reduce them to low levels, for example, by filtering electrically the inlet and outlet gases in motors.

I am indebted to the Swedish Cancer Society for economic support. Advice by Dr. R. Siksna on the charge collection chamber is also gratefully acknowledged

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GEOCHEMISTRY

Apparent Geochemical Association of Bismuth and Thallium

THE geochemical association of certain pairs or groups of elements has been noted by several authors, and a classical example is the rubidium/thallium relationship which has been described by Ahrens[1]. In order that such a coherence should be established, it is necessary that not only should a large number of

accurate analyses be available but also that these data should be obtained for each element on identical geological specimens.

Until recently, very few data have been available for the abundance of bismuth in silicates due to the lack of analytical methods sufficiently sensitive for its determination at its low concentration levels in such rocks. However, a new method has been developed[2-4] in which this element has been determined spectrochemically after previous enrichment by an anion-exchange procedure. It has also been possible to determine simultaneously thallium and other elements, and abundance data for these two elements have been obtained for some sixty rock specimens. In addition to this work, Ehmann and Huizinga[5] have determined bismuth and thallium at very low concentrations in chondrites by a neutron activation method. The only other simultaneous analytical data for bismuth and thallium in silicates are those of Preuss[6], who estimated these elements by a spectrochemical distillation technique.

I have collated all the available data and noted a surprising apparent relationship between bismuth and thallium, and this is shown in Fig. 1, where a log/log plot of thallium concentrations as a function of bismuth concentration is shown. The points on the diagram for Goldschmidt[7] and the Noddacks[8] are estimates only, and one of my points represents the average of a suite of 19 dolerites from the Jagersfontein diamond mine, South Africa, of which some of the individual analyses show greater scatter than the other points on the graph. All the data include a comprehensive range of silicate rocks from granites to ultra-basics.

The apparent coherence between bismuth and thallium is difficult to explain but it is interesting to note that Oftedal[9] has determined both bismuth and thallium in several samples of galena where both elements are found to be highly concentrated and has reported maxima of 500 p.p.m. thallium and 1,000 p.p.m. bismuth. Goldschmidt[7] has suggested that the enrichment of these metals in lead minerals may be due to the replacement of two atoms of lead by one atom each of bismuth and thallium. The ionic radii of lead, bismuth and thallium are shown in Table 1.

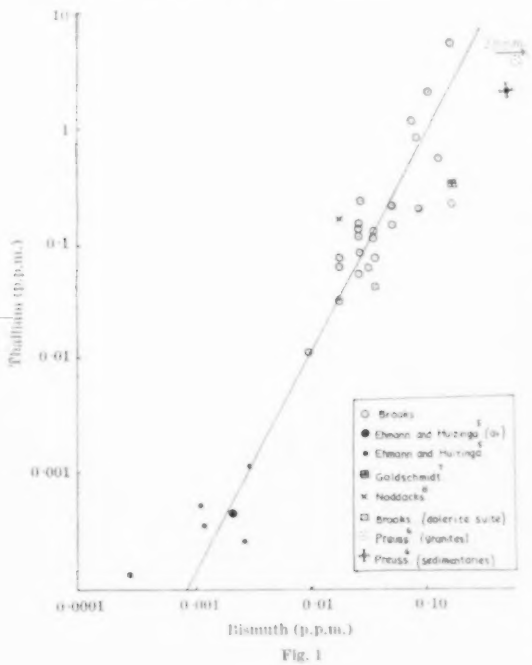

Fig. 1

Table 1. Ionic Radii of Bismuth, Thallium and Lead

Element	Ionic radius
Tl^{+}	1·49 Å.
Bi^{+++}	1·09 Å.
Pb^{++}	1·32 Å.

The belief that lead may be the common link between thallium and bismuth is strengthened by consideration of the abundance of lead in silicates[10] where the lead concentration increases regularly from about 3 p.p.m. in ultra-basics to about 20 p.p.m. in granites. It is true that lead is not a major constituent of most rocks; but since its abundance is very much greater than that of either bismuth or thallium, it is possible that the mechanism of a major element camouflaging a trace element will apply in this case. It is noteworthy that thallium, bismuth and lead are the heaviest three non-radioactive elements, and this may have some significance for their apparent relationship.

Therefore, it may be possible to account for the apparent thallium/bismuth coherence from the premise that one atom each of bismuth and thallium replace two atoms of lead, since the ionic radii of these three elements do not preclude this replacement.

As more data become available for the relative abundances of bismuth and thallium, it should be possible to establish further this apparent relationship.

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OCEANOGRAPHY

Overflow of Cold Deep Water across the Iceland–Greenland Ridge

Increasing attention has been given in recent years to the overflow of cold bottom water, formed by winter cooling in the Norwegian Sea, across the various submarine ridges separating the basin of the Norwegian Sea from that of the Atlantic Ocean. In June 1960, under the auspices of the International Council for the Exploration of the Sea, nine ships from five different countries investigated the overflow across the Iceland–Faroe Ridge by means of a series of parallel hydrographic sections between Iceland

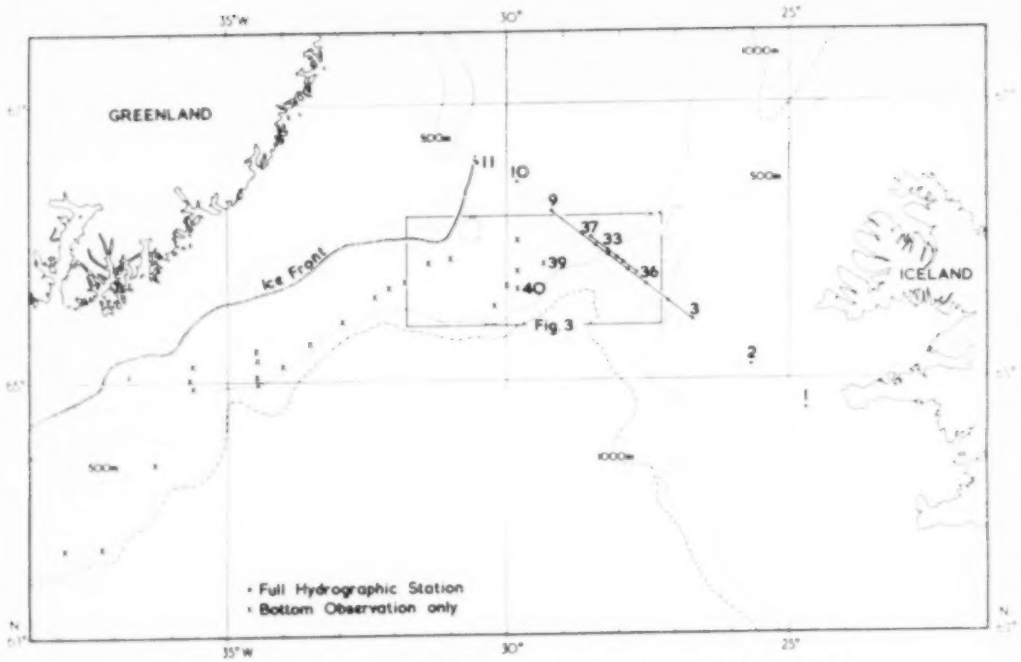

Fig. 1. R.V. *Ernest Holt* Cruise VI 1960: Location of stations worked in the Denmark Strait

and the Faroes, and made direct current measurements at a number of strategic points.

In August 1960, the English Fishery Research Vessel, *Ernest Holt*, which had participated in the Iceland–Faroe Ridge Survey, worked a hydrographic section across the Denmark Strait (Fig. 1), along the submarine ridge joining Iceland to Greenland, and made direct measurements of the current near the bottom at a selected point along this section. The section was worked on August 15 and 16 from a position some sixteen miles from the Iceland coast to the ice front, approximately eighty miles from the Greenland coast. In the deepest part of the section, that is, below 450 metres, where any overflow taking place would be expected, the coldest bottom water found was 2·5° C. at station 7. Fig. 2*a* shows the central and deepest part of the section.

On the completion of the section, the *Ernest Holt* returned to the position, as near as could be determined, of station 7 to anchor in 550 metres depth (station 33) and make direct measurements of the current near the bottom. It was found that the bottom temperature was now 0·1° C. The time interval between the taking of the bottom temperatures

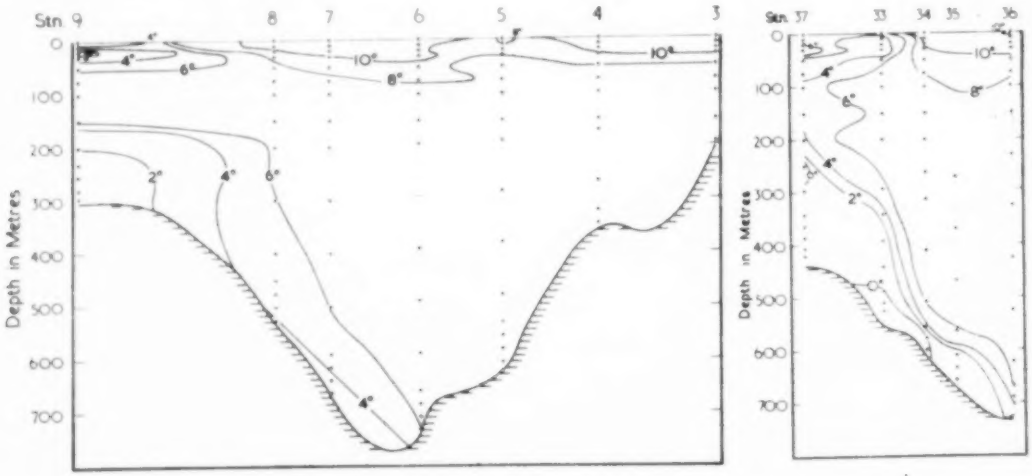

Fig. 2. (*a*) Iceland–Greenland Section (1600 hr. G.M.T. August 15–1700 hr. August 16): temperature (° C.). (*b*) Part of Iceland–Greenland Section (1300 hr. G.M.T.–2200 hr. August 17): temperature (°C.)

at stations 7 and 33 was 20 hr. Direct current observations (ten in a period of 14 hr.) were then made within five metres of the bottom by means of a Carruthers' Pisa current indicator[1]. The preliminary analysis of the observations shows a residual current of 0·3 knot in a direction 250° true when the tidal current is eliminated.

Immediately the current observations were completed at 1300 hr. G.M.T. on August 17, the part of the section previously worked in the immediate vicinity of station 7 was repeated in an attempt to delimit the extent of the cold bottom water encountered at station 33 during the measurement of the current. Fig. 2*b* shows the results of this.

After this part of the section had been repeated, a bottom temperature survey on the fishing banks to the west and south of the section was commenced, during which the front of the advancing cold bottom water was identified as lying between stations 39 and 40, sixteen nautical miles apart, at 0430 hr. on August 18, as shown in Fig. 3. The rate of advance of the front of the cold water can be estimated between two limits from the knowledge of the interval of time during which it passed station 7 and the two positions between which it was situated at 0430 hr. on August 18, assuming the axis of flow to have been along the line joining stations 33, 39 and 40. The limits thus determined are 0·55 knot and 1·4 knots, and the line of the axis of flow thus assumed is approximately 255° true. This direction agrees almost exactly with that of the current measured at station 33 and, although both limits of the rate of advance of the cold water front exceed that of the observed current, the lower limit is of the same order of magnitude.

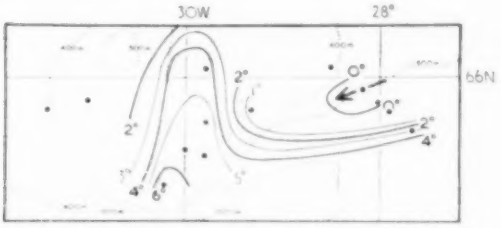

Fig. 3. Bottom temperature distribution (° C.) on the south-western side of the Iceland Greenland Ridge (1300 hr. G.M.T. August 17–1600 hr. August 18)
Bottom residual current, → ●—; ●, station

An analysis of the salinity values in the deeper layers of stations 7 and 33 shows the sudden decrease in temperature to be the result of a renewal of the overflow of cold Norwegian Sea deep water across the Iceland Greenland Ridge. This finding adds support to the hypothesis of Cooper[2] that the overflow is intermittent and takes the form of a series of discrete boluses. It is also in agreement with one of the findings of the Iceland Faroe Ridge Survey of June 1960, namely, that the bottom temperature on the southern side of these ridges can change rapidly. It is perhaps of significance in a consideration of the factors controlling the overflow that the surface front between the warm Atlantic water and the cold southward-flowing East Greenland Current apparently shifted towards the south-east between the two occasions when the section was worked. As a result of this, on the first occasion when there was little evidence of any overflow, station 7 was located in the warm Atlantic water, but when the *Ernest Holt* returned to station 33 and found a strong overflow it was located in the cold East Greenland Current.

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LIMNOLOGY

A Second Lake with Old Sea-Water at its Bottom

Four years ago I directed attention to a Lake (Rorholtfjorden, part of Lake Tokke, in southern Norway) with trapped sea-water[1]. The surface altitude of that Lake is 60 m. above sea-level, and the estimated age of its bottom waters some 6,000 years, that is, of the marine salts contained in them; the present bottom waters probably possessing one-half of the salinity of those originally isolated.

While there are a large number of land-locked waters still having some communication with the sea, there are very few where bottom waters have been completely isolated, and not washed out through admixture with fresh water layers above. Until their discovery in Lake Tokke, salt bottom waters were known only from lakes near sea-level, where isolation through post-glacial land rise must have occurred but recently.

Since my communication, work in progress on Lake Tokke has led to some results, especially concerning isotope distribution in sediments.

Further research made it very desirable to find a second lake with old sea-water, and finally, my collaborator, Mr. H. V. Sovik, in January 1961, discovered such a lake, Botnvatn, in the district of Salten, northern Norway (67° N.), the altitude of the lake surface being 12 m.

Lake Ovrevatn, a land-locked fjord[2] near Botnvatn, with an average height of its water-level of about 2 m. above daily ebb, is at the point of being isolated from the sea. We can thus assume a land rise since the isolation of Botnvatn, of about 10 m., and that the isolation probably took place some 3,000 years ago.

Botnvatn is 113 m. deep, with salt waters from 102 m. downward. Hydrography is very similar to that of Lake Tokke, where salt waters extend from 134 m. to the bottom (147 m.). A comparison may be made between the salt-water layers of the two lakes:

	Tokke, 144 m.	Botnvatn 111 m.
Chlorine (mgm./l.)	9·24	7·26
Salinity (gm./kgm.)	16·71	13·14
Temp. (° C.)	5·20	4·75

As is the case in Lake Tokke, the salt bottom waters contain enormous amounts of methane, and bubble violently when brought to the surface. We thus have to face the same problem as in Lake Tokke, that with decrease in pressure the release of methane, also within the sediments, makes it very difficult to secure undisturbed samples of the bottom deposits.

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CHEMISTRY

Vibration Frequency and Ionization Potential: Halide Molecules

It has been observed that a systematic correlation is possible between the sum of normal vibration frequencies of a molecule and the first ionization potentials of its constituent atoms.

The sum, $\Sigma\nu$, of all the normal frequencies (degeneracies, if any, included) of a molecule RX_n, where X is a halogen and R a molecular group, has been found to be a linear function of the sum of the first ionization potentials, ΣI_x, of the halogen atoms occurring in the molecule. A plot of $\Sigma\nu$ for a group of molecules with the same R, but with all possible halogen substitutions against ΣI_x is thus a straight line. Preliminary tests, indicating the validity of the relation, have been made on fifteen CX_4, nine CHX_3, six CH_2X_2, four CH_3X, nine C_2X_4, seven C_2HX_3, five $C_2H_2X_2$, three C_2H_3X, ten $^{11}BX_3$, ten $^{10}BX_3$ and three XCN type molecules.

It is also observed that the $\Sigma\nu$ values of two similar sequences of halides are linearly related:

$$\Sigma\nu(RX_n) = \alpha\Sigma\nu(RX_n) + \beta$$

provided both the series contain the same number of halogens and the corresponding members are compared.

Details of the work and results of allied investigations will be reported elsewhere.

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Delayed Gas Evolution from Passive Films formed in the Kolbe Reaction

During the course of electrochemical kinetic studies on the Kolbe reaction, we have observed a remarkable phenomenon, the details of which are recorded here. The classical Kolbe reaction involves the anodic electrolytic synthesis of hydrocarbons from solutions of salts of appropriate aliphatic carboxylic acids. As a model system for preliminary investigations of the electrochemical kinetics of this reaction, we have examined the anodic reaction which occurs in the electrolysis of a solution of potassium formate in pure anhydrous formic acid; in this case 1 mole of carbon dioxide is evolved in the passage of two Faradays.

During steady-state electrolysis of the above solution at platinum, gold and palladium electrodes, the only gas evolved is carbon dioxide. The overall reaction is hence formally[1]:

$$2HCOO^- \rightarrow HCOOH + CO_2 + 2e$$

On interrupting the current at platinum and gold electrodes, the gas evolution ceases immediately in the normal way. However, on interrupting the current at a palladium electrode, the gas evolution initially ceases, but is then followed by a further burst of gas from the surface after a delay period of up to 5 sec., this gas evolution occurring in the complete absence of current-flow. The effect at palladium is quite reproducible and is best observed at a current density greater than 10^{-1} amp./cm.^{2} in 5-M solutions of potassium formate in formic acid (pre-saturated with carbon dioxide) at 5° C. Although carbon dioxide is evolved at platinum and gold with the same current efficiency (about 90 per cent) as at palladium, the delayed gas evolution is not observed, and the effect hence arises from some property of the palladium anode. No hydrogen is evolved as might be expected by analogy with the coupling reaction occurring with acetic and other aliphatic acids, but this is understandable since any H radicals generated by the anodic decarboxylation will ionize rapidly at a rate of at least 10^{19} amp./cm.^{2} at the high anodic potentials (about 1·2 V. with respect to the hydrogen electrode in the same acid solution) required for significant rates of electrolysis of the formic acid. Hence it is improbable that hydrogen produced in the decarboxylation step and taken up into the surface regions of the palladium is responsible for the effect, and in fact the coulombic yields of carbon dioxide gas by continuous and repeatedly interrupted polarization are identical within experimental error and no hydrogen is detectable by chemical or gas chromatographic means under either set of conditions of polarization.

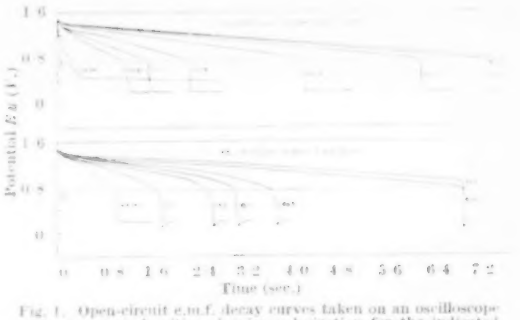

Fig. 1. Open-circuit e.m.f. decay curves taken on an oscilloscope at two current densities of prior polarization for the indicated times (sec.).

Rapid ciné-photography of the palladium surface with a simultaneous recording of the moment when current stops flowing has enabled the delay-times in gas evolution in interrupted polarization experiments to be measured with some precision to about 0·1 sec. The delay-time in the gas evolution after the current stops is found to be a function of the time of previous anodic electrolysis up to periods of about 5 min. This suggests that the anodic electrolysis

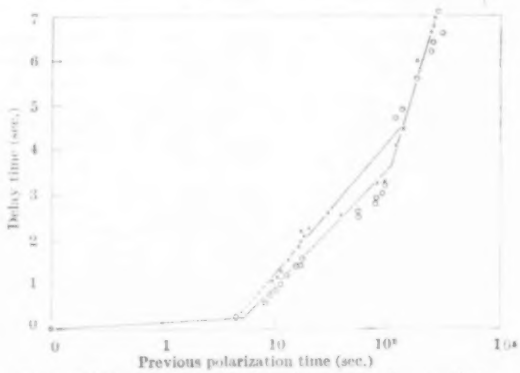

Fig. 2. Relationship of both the delay in open-circuit gas evolution (from ciné photography) and the potential delay to the period of prior anodic polarization at 10^{-2} amp./cm.^{2}. ○, delayed gas evolution; ×, potential delay; 5 M HCOOK/HCOOH

forms a relatively thick film of a surface palladium formate (possibly non-stoichiometric[2,3]) at the electrode, and, after net current ceases to flow, this film breaks down auto-catalytically with evolution of carbon dioxide. The formation of this film appears to be analogous to that of passive films formed anodically, for example, in aqueous solutions at nickel and iron. Determinations of the galvanostatic charging and open-circuit decay curves, using a cathode ray oscilloscope, for the polarized palladium and platinum electrodes indicate the formation of surface films as shown in Fig. 1. The pseudo-capacity associated with the film at palladium is much greater (10–50 times) than that at platinum, and this is evidently the reason why the delayed decomposition is observable at the former metal although it may still occur but not be visible at platinum or gold. We believe that the effect is larger at palladium than at the other metals since palladium is less noble than gold or platinum, so that palladium has a greater susceptibility to anodic oxidation. The delay in the open-circuit decay trace of e.m.f. as a function of time is found to depend on the time of previous anodic polarization, as also observed with the delay in visible gas evolution on open-circuit. The delay in the e.m.f. decay curve, in fact, is directly related to the delay in the open circuit gas evolution as shown in Fig. 2: both effects appear to be related to the thickness of the anodically formed layer. Less spectacular self-discharge effects with non-delayed evolution of oxygen occurring over much longer periods of time are known in oxide electrode systems and have been treated in detail in some of our previous papers[2–4]. Visible delayed gas evolution effects are not observed when the true Kolbe coupling reaction is proceeding, for example, in the electrolysis of trifluoroacetic acid, although galvanostatic charging curves again indicate formation of surface films but of thicknesses much less than those found at palladium in the formic acid solutions.

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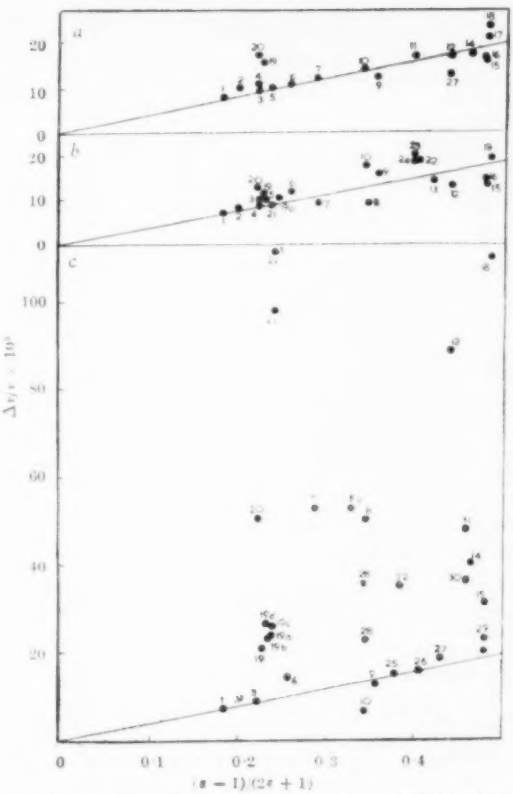

Fig. 1. Relative frequency shift at: *a*, ν C—Cl (asym.) of *cis*-dichloroethylene; *b*, ν C=O of acetophenone; *c*, ν N—H of pyrrole in dilute solution as a function of the dielectric constant of the solvent

Solvents: 1, *n*-Hexane; 2, cyclohexane; 3, carbon tetrachloride; 4, cyclohexene; 5, tetrachloroethylene; 6, carbon disulphide; 7, di-*n*-butyl ether; 8, diethyl ether; 8*a*, isopropyl ether; 9, chloroform; 10 bromoform; 11, methyl iodide; 12, pyridine; 13, methylene chloride; 14, acetone; 15, acetonitrile; 16, nitromethane; 17, dimethyl formamide; 18, dimethyl sulphoxide; 19, benzene; 19*a*, toluene; 19*b*, *m*-xylene; 19*c*, *p*-cumene; 19*d*, mesitylene; 20, dioxan; 21, triethylamine; 22, pyrrole; 23, aniline; 24, methylene iodide; 25, chlorobenzene; 26, *sym*-tetrachloroethane; 27, 1:2 dichloroethane; 28, anisole; 29, nitrobenzene; 30, acetophenone; 31, cyclohexanone; 32, ethyl acetate

Dielectric and Dipolar Interaction Theories of Solvent-induced Infra-red Frequency Shifts

Considerable attention is at present being focused on the effect of solvent environment on infra-red frequencies[1–3]. The early dielectric constant treatment of Kirkwood, Bauer and Magat[4] (KBM), long known to be inadequate for the group frequencies which had been studied in any detail, namely, N—H (ref. 5) and C=O (ref. 6), has been followed by the dipolar association theory of Bellamy, Hallam and Williams[1] (BHW). They have shown that the solvent shift of a range of X—H stretching frequencies (where X = boron, carbon, nitrogen, oxygen, sulphur, halogens) can be fully accounted for in terms of solute-solvent dipolar interactions and that the bulk dielectric constant of the medium plays an insignificant part. The same theory is also able to explain the major part of the shifts exhibited by X=O chromophores[2]. Other factors must, however, have some influence on these dipoles as the slopes of the BHW plots obtained on plotting the relative shifts against a common standard[2] do not parallel other measures of bond polarity as would be predicted on the basis of the dipolar association theory and as has been demonstrated for X—H dipoles[1], in particular, N—H (ref. 7). Buckingham's elegant extension of the dielectric theory has been tested and extended by Caldow and Thompson[3] in their detailed evaluation of carbonyl and cyanide shifts. They suggest that both dielectric and specific interaction effects operate, and, by considering interaction terms, based on values of Taft's σ^* inductive factors, conclude that the dielectric factor contributes about 30 per cent of the total $\Delta\nu$ exhibited by C=O dipoles. Norrish[8] has approached the problem via solute-solution interaction energies in terms of the internal latent heats of solute and solvent and the heat of mixing. However, as he points out, lack of data does not permit a rigorous test of his relationship.

We are at present examining the effect of solvent environment on C—halogen frequencies. In general, as might be anticipated for a dipole the end of which most readily available for association is of the same sign, these follow the same overall pattern of solvent behaviour as that exhibited by C=O. The relative shift is also of the same order as for C=O, but a theoretical breakdown of this into the various contributions leads us to the conclusion that with these dipoles the dipolar interaction and dielectric factors play almost equal parts. The most striking outcome is the reasonable success of the KBM treatment, a typical example being shown in Fig. 1*a*, which also includes typical examples of an N—H frequency (Fig. 1*c*), taken from the data of Josien *et al.*[5], and extended by us[1], and a carbonyl frequency (Fig. 1*b*) plotted from the data of Bellamy *et al.*[2], with some additional points from these laboratories. It is immediately apparent that C—halogen KBM plots represent the most satisfactory plots to date of this function. Our analysis in terms of Buckingham's theory[8] as extended by Caldow and Thompson[3] enables us to account for the deviations from the KBM relationship which are found with highly polar solvents such as dimethyl formamide and dimethyl sulphoxide, in terms of specific dipolar interactions.

It is clear that in the development of theories of solvent effects it must be appreciated that neither of the two major factors which contributes to infra-red solvent shifts can be ignored, and that their relative significance varies from case to case, being dependent as much on the particular dipole absorber as on the solvent medium itself.

We are grateful to the Hydrocarbon Research Group of the Institute of Petroleum for financial support and to the Imperial Smelting Corporation, Ltd., for gifts of fluoroform and carbon tetrafluoride.

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A New Synthetic Route to Dialkylphosphinous Chlorides

Preparative methods for dialkylphosphinous chlorides are few in number, and frequently give unsatisfactory yields or require techniques unsuitable for such problems as the synthesis of radioactively labelled compounds of high activity[1–3]. A recently described reaction for the preparation of alkylphosphonous dichlorides[4] has been shown to be adaptable to the preparation of dialkylphosphinous chloride in a single-flask reaction with good yield.

It has been found that alkylphosphonous dichlorides will form a complex with aluminium chloride and an alkyl halide in the same manner as does phosphorus trichloride[5]. Solution of this complex in an electron-donating solvent, for example diethyl phthalate (DEP), followed by reduction with powdered antimony or, preferably, powdered zinc, gives good yields of dialkylphosphinous chloride on distillation.

$$RCl + R'PCl_2 + AlCl_3 \rightarrow [RR'PCl_2]^+[AlCl_4]^-$$

$$\xrightarrow[\text{Zn or Sb}]{\text{DEP}} RR'PCl + [AlCl_3][DEP] + ZnCl_2 \text{ or } SbCl_3$$

The mixed and symmetrical products prepared by this route are given in Table 1.

Table 1

Compound	b.p./mm.	n_D^t	Yield (per cent)
$(CH_3)_2PCl$	70/690	—	45
$(c\text{-}C_6H_{11})_2PCl$	69/33	1·4745(25°)	68
$(C_6H_{11})_2PCl$	92/4	1·4771(0°)	46
$(CH_3)(ClCH_2)PCl$	67/98	1·5140(20°)	73
$(CH_3)(ClCHCH_3)PCl$	90/100	—	41
$(CH_3)(o\text{-}C_6H_4)PCl$	82–85/208	—	66
$(ClCH_2)_2PCl$	76/22	—	22

Full details will be reported elsewhere.

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BIOCHEMISTRY

Uptake of Deoxyribonucleic Acid (DNA): a Special Property of the Cell Nucleus

According to the concept of metabolic stability, DNA is synthesized only before cell division and during the formation of polyploid nuclei. Thus the incorporation of labelled precursors is generally considered to be a measure of DNA synthesis and, consequently, of proliferative activity of the cell population in question.

In the light of recent findings, this assumption does not have absolute validity. Pelc has observed incorporation of adenine-^{14}C and ^{3}H-thymidine into the epithelium of the vesica seminalis in amounts exceeding by 20–80 times the DNA value required for cell division[6,7]. He interprets his findings as metabolic activity of DNA connected with some cellular functions of non-growing differentiated epithelium[10]. In the case of phosphorus, however, no exchange was found in the DNA of single non-dividing cells[7,8].

I have observed DNA labelling in resting cells of bone marrow, thymus and spleen after transfusion of homologous lymphocytes labelled with phosphorus-32. Control experiments using phosphorus-32 as inorganic phosphate were mostly negative, and thus the possibility of metabolic exchange of phosphorus-32 in the DNA molecule itself was excluded[1]. It is therefore assumed that the resting cells of the recipient took up the whole DNA-phosphorus-32 or a large part of it from nuclear debris of injected donor cells.

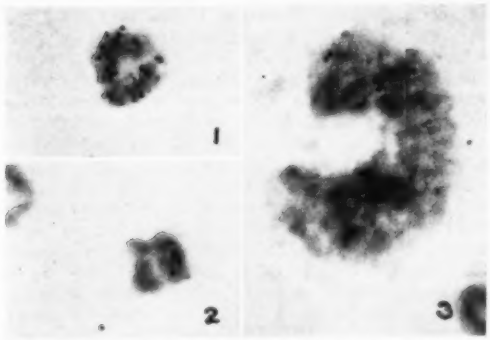

Fig. 1. Autoradiographs of the recipient's bone marrow cells 2 hr. after the application of lymphocytes labelled with phosphorus-32, showing labelling of (1) ring-shaped nucleus of a granulocyte; (2) one segment of the granulocyte nucleus; (3) a megakaryocyte in which the label occurs only in one half of the nucleus. Feulgen, squash. (× 1,725)

The distribution of the label in resting nuclei was examined in greater detail, and the preliminary results are given here.

Homologous lymphocytes labelled with phosphorus-32 were obtained from the thymuses of male *H* mice injected with 25 μc. of inorganic phosphorus-32, 21 hr. before being killed. The thymuses were suspended in isotonic Hanks's solution, the cell suspension was washed and injected intravenously into 10 males of the same mouse strain 24 hr. after total-body irradiation with a dose of 800 r.; X-rays were delivered at the rate of 60 r./min. (180 kV., 15 m.amp., filters 1 mm. aluminium and 0·5 mm. copper, target distance 45 cm.). Each irradiated mouse was given 0·1 mgm. heparin intraperitoneally and 1 ml. of suspension containing 50 million cells with a total radioactivity of 0·01 μc. per ml. The recipients were killed 2 and 6 hr. after the administration of cells. Their bone marrow fixed with acetic alcohol and stained with Feulgen was squashed in accordance with Sachs's method[11]. The non-DNA phosphorus was removed from the preparations by Feulgen acid hydrolysis[6]. The specimens were covered with liquid '*A*-2' emulsion, exposed for 1 month and developed in *D*19.

Labelled cells were found in the bone marrow of the recipients singly and in groups. The Feulgen reaction made possible the differentiation of some cell types only: granulocytes, myelocytes, reticular cells, megakaryocytes, and mononuclear cells of the lymphocyte or erythroblast series. The label occurred in the nuclei of all the types of cell mentioned. In the case of nuclei of small mononuclear cells, the grains of emulsion were evenly distributed. In the granulocytes the distribution of grains was convincing enough to prove radioactivity in the nucleus but not in the cytoplasm (Fig. 1). In some granulocytes only one of the nuclear segments was labelled (Fig. 2). The megakaryocytes often took up the label only in one part of their nucleus (Fig. 3). In the nuclei of the reticular cells, most of the grains were localized above the heterochromatin associated with the nucleolus.

The presence of DNA-phosphorus-32 in the nuclei of granulocytes, which are non-dividing differentiated cells, as well as the accumulation of label only in certain areas of the nuclei of megakaryocytes or reticular cells, exclude the possibility of phosphorus-32 in the form of simpler precursors having been utilized in DNA synthesis and/or in metabolic turnover. The distribution of label in the nuclei gives sufficient evidence that a whole DNA molecule or large portions of it penetrate through certain places on the nuclear surface. Its entrance is probably facilitated by the same mechanisms that are responsible for the penetration of cytoplasmic material giving rise to intranuclear inclusions[7]. The ensuing process of incorporating the DNA which has penetrated into certain nuclear structures remains open to further investigation. In the heterochromatin regions of reticular cells, the label persisted for 48 hr. after the administration of labelled cells[8].

Although it is not possible at present to decide whether incorporated homologous DNA performs its proper biological function, this seems to be the case with autologous DNA. The property of the cell nucleus of taking up DNA from the intercellular environment supports the hypothesis that the lymphocyte nucleic acids are re-utilized by originating cells of the ensuing lymphocyte generation. This has been hitherto based only on indirect biochemical data[1] and cytological findings in lymph node cultures[12] and in spleen lymphoid tissue[2,3].

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Prevention of Fatty Liver due to Threonine Deficiency by Moderate Caloric Restriction

Rats fed a diet containing 9 per cent casein supplemented with sulphur-containing amino-acids and choline develop moderately fatty livers, but if the diet is supplemented with threonine, the accumulation of fat is reduced[1,2]. Evidence that fat synthesis is accelerated in rats fed the threonine-deficient diet was obtained by measuring the incorporation of acetate-1-^{14}C into liver and carcass fat[2]. This suggested that rats fed this low protein diet consume an excess of calories in relation to their intake of balanced protein and that the extra calories are used for the synthesis of fat.

The present communication describes observations made on the effect of caloric intake on the production of fatty liver caused by threonine deficiency. A moderate restriction of caloric intake prevented the development of fatty livers in rats fed the threonine-deficient diet, but an equivalent restriction of caloric intake did not prevent the accumulation of liver fat in rats fed a choline-deficient diet.

Male weanling albino rats of the Wistar strain were used. The experiments consisted of two series; in one threonine-deficient diets were fed, in the other choline-deficient diets. The composition of the experimental diets is presented in Table 1. In both series, the control groups of rats were fed the respective basal diets *ad libitum*, and food consumption

Table 1. Composition of Diets

	Threonine-deficient diets			Choline-deficient diets	
	Basal	70 per cent calories	50 per cent calories	Basal	70 per cent calories
Casein	90	90	90	85	85
DL-Methionine	3	3	3	—	—
Sesame oil	50	50	50	50	50
Salt mixture	40	40	40	40	40
Vitamin mixture	4·5	4·5	4·5	4·5	4·5
Choline hydrochloride	1·5	1·5	1·5	—	—
Cholesterol	—	—	—	5	5
Sucrose	815	569	395	815	515
Feed ratio*	1	0·7	0·5	1	0·7

* Relative caloric intakes when diets were fed in quantities that provided equal amounts of protein.

was measured daily. The other groups of rats in each series were fed the same amounts of protein and amino-acids as their respective control groups consumed, but the caloric intakes were 70 or 50 per cent of their respective control groups. At the end of two weeks the rats were killed, their livers were removed and fat was extracted with ether from the dried and finely powdered liver.

As shown in Table 2, the fat content of the livers of the control rats in the threonine-deficient series was 20·3 per cent on a dry weight basis whereas the value for the rats that received 30 per cent less calories was 13·3 per cent, within the normal range. Thus, a moderate reduction in caloric intake with an equal intake of protein prevented the fatty infiltration without appreciably reducing growth. Reduction of caloric intake to 50 per cent of that of the control group further decreased liver fat content (9·2 per cent) but also retarded growth. These results suggest that the balance between amino-acid and caloric intake is important in controlling liver fat accumulation.

Table 2. Effect of Caloric Intake on Fat Content of the Livers of Rats fed on Threonine- or Choline-Deficient Diets

	Threonine deficiency			Choline deficiency	
	Basal	70 per cent calories	50 per cent calories	Basal	70 per cent calories
Gain for 2 weeks (gm.)	35·5	32·1	16·2	17·0	6·8
Protein intake for 2 weeks (gm.)	11·4	11·4	11·4	8·8	8·8
Caloric intake for 2 weeks	518	363	259	427	299
Liver fat (per cent*)	20·3 ± 3·2†	13·3 ± 0·3	9·2 ± 0·2	30·1 ± 3·6	28·6 ± 4·0

* Liver fat is expressed as percentage of dry liver.
† S.E.

This effect was not observed when the fatty liver was caused by choline deficiency (Table 2). The growth of the group fed the choline-deficient diet and 30 per cent less calories than the control group was markedly reduced; however, there was no significant fall in liver fat content. Best and Ridout[4] found that the fatty liver of choline deficiency was prevented by severe, but not by moderate, caloric restriction.

A reduction in caloric intake would decrease the quantity of precursors for fat synthesis. If a fatty liver were caused by an acceleration of fat synthesis due to an excessive carbohydrate intake a reduction in caloric intake would be expected to decrease the fat accumulation. However, if the fatty liver were primarily a result of impaired transport of fat, a reduction in caloric intake would not be expected to affect fat accumulation so much. In this connexion, these results are in agreement with those which indicated that there is an accelerated incorporation of acetate-1-^{14}C into liver fat in threonine-deficient rats[3].

The fatty liver caused by feeding rats a low protein diet that is primarily deficient in threonine appears to be a result of a disproportionately high intake of calories in relation to the intake of balanced protein. This emphasizes the need for further work on the relationship between protein and caloric utilization on animals and subjects having low intakes of protein.

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Polypeptide Chains of Hæmoglobin A_2

Hæmoglobin A_2 (Hb-A_2), first described by Kunkel and Wallenius[1], is a minor component found in normal adult hæmolysate which has an electrophoretic mobility slower than Hb-A at alkaline pH. Several variants of Hb-A_2 have been described and these now fall into two groups. While the minor hæmoglobins of one group can occur when Hb-A is normal, for example, Hb-A'_2 (ref. 2) and Hb-B_2 (ref. 3), those of the other group are always associated with α-chain variants of Hb-A. Shooter, Skinner, Garlick and Barnicot[4] described a minor hæmoglobin variant of the latter group which they called Hb-G_2 in an individual carrying Hb-G_{Ibadan}. Since the charge relationship between Hb-G_2 and Hb-G_{Ib} was similar to that between Hb-A_2 and Hb-A, Gammack, Huehns, Shooter and Gerald[5] suggested that Hb-G_2 was the naturally occurring hybrid of Hb-A_2 and Hb-G_{Ib}. This hypothesis implied not only that Hb-G_{Ib} has abnormal α_2 sub-units, but also that Hb-A_2 differs from Hb-A only in the composition of the non-α_2 sub-unit and has the molecular formula $\alpha_2^A\delta_2^A$. It has already been shown[6] that Hb-G_{Ib} consists of normal β_2^A and abnormal $\alpha_2^{\prime\prime}$ sub-units, and the results now reported are consistent both with the above formula for Hb-A_2 and with the suggestion that Hb-G_2 carries the abnormal sub-unit of Hb-G_{Ib} and the specific sub-unit of Hb-A_2.

Hybridization experiments were carried out using a microscale adaptation[5] of the original recombination method developed by Itano and Robinson[6]. Whereas most variants of Hb-A give satisfactory hybrid formation after exposure to pH 4·7 for 4 hr.[7] no new hæmoglobin species could be detected in similar experiments with Hb-A_2. However, if the time of dialysis against acetate buffer at pH 4·7 was extended to 72 hr. or more, amounts of hybrid hæmoglobins sufficient for their detection also formed with Hb-A_2. Thus, when mixtures of the isolated hæmoglobins Hb-A_2 and Hb-G_{α} were dissociated for these longer

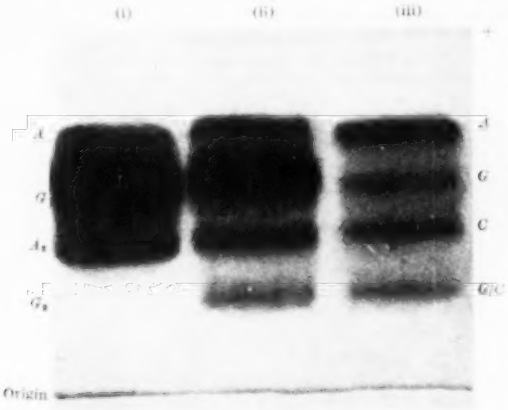

Fig. 1. Hybridization of hæmoglobins A_2 and $G_{Hr.}$ Starch-gel analysis in the discontinuous system. Migration time 2 hr., *o*-dianisidine stain. (i) Hb-A_2 + Hb-$G_{Hr.}$ untreated mixture; (ii) Hb-A_2 + Hb-$G_{Hr.}$ dissociated at *p*H 4·7 for 96 hr. and then recombined; (iii) Hb-*A*, $G_{Hr.}$, *C*, *G*/*C* marker

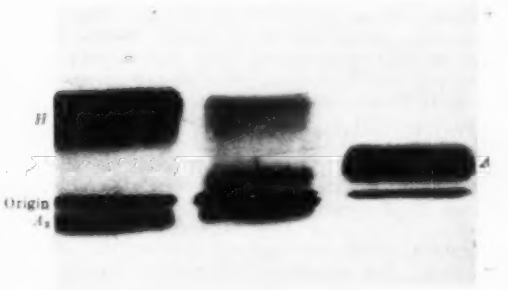

Fig. 2. Hybridization of hæmoglobins A_2 and *H*. Starch-gel analysis in phosphate buffer, gel *p*H 7·4. Migration time 2 hr., *o*-dianisidine stain. (i) Hb-A_2 + Hb-*H* untreated control mixture; (ii) Hb-A_2 + Hb-*H* dissociated for 72 hr. and then recombined; (iii) Hb-*A* marker
(The movement of the new zone (Hb-*A*) in (ii) is slightly decreased by the more concentrated Hb-A_2 zone migrating towards the opposite electrode when compared with the Hb-*A* marker (iii))

periods and then recombined at *p*H 6·8, a new hæmoglobin zone migrating more slowly than Hb-A_2 and in the position of Hb-*G*/*C* appeared and some intensification of the Hb-*A* zone occurred (Fig. 1). With isolated Hb-*H*, Hb-A_2 gave Hb-*A* (Fig. 2). No new species appeared when Hb-A_2, Hb-G_{α} or Hb-*H* by themselves or a mixture of Hb-A_2 and Hb-*S* were dissociated and recombined in parallel experiments.

The formation of Hb-*A* in the hybridization with Hb-*H* suggests that Hb-A_2 has α_2^A sub-units similar to those found in Hb-*A*.

$$\underset{\text{Hb-}A_2}{\alpha_2^A\delta_2^{A_2}} + \underset{\text{Hb-}H}{\beta_4^A} \rightarrow \underset{\text{Hb-}A}{\alpha_2^A\beta_2^A} + \underset{\text{Hb-}A_2}{\alpha_2^A\delta_2^{A_2}} + (\beta_2^A + \delta_2^{A_2})$$

(The fate of the sub-units enclosed in brackets has not been determined.)

The charge difference between Hb-A_2 and the new hæmoglobin species formed in the dissociation and recombination experiment with Hb-$G_{Hr.}$ is similar to that between Hb-*C* and Hb-*G*/*C*. The structural difference between these two is the replacement of the α_2^A sub-unit of Hb-*C* with an α_2^G sub-unit[4]. It therefore follows that the difference between Hb-A_2 and the new hæmoglobin formed in the hybridization experiment with Hb-$G_{Hr.}$ could also be the replacement of an α_2^A sub-unit in Hb-A_2 by an α_2^G sub-unit. The reaction may then be written as follows:

$$\underset{\text{Hb-}G}{\alpha_2^G\beta_2^A} + \underset{\text{Hb-}A_2}{\alpha_2^A\delta_2^{A_2}} \rightarrow \underset{\text{Hb-}A}{\alpha_2^A\beta_2^A} + \underset{\text{Hb-}G}{\alpha_2^G\beta_2^A} + \underset{\text{Hb-}A_2}{\alpha_2^A\delta_2^{A_2}} + \underset{\text{Hb-}G_2}{\alpha_2^G\delta_2^{A_2}}$$

Charge difference from Hb-*A*:

$$+2 \qquad +4 \qquad 0 \qquad +2 \qquad +4 \qquad +6$$

These hybridization experiments are, therefore, consistent with the hypothesis that Hb-A_2 has the general formula $\alpha_2^A\delta_2^{A_2}$.

Raper, Gammack, Huehns and Shooter[5] have suggested from the study of two individuals carrying the four hæmoglobins *A*, $G_{Hr.}$, *C* and $G_{Hr.}$/*C* that the last stage of hæmoglobin synthesis is the combination of α_2 with β_2 sub-units. If this also applies to Hb-A_2, in this instance α_2^A sub-units combining with $\delta_2^{A_2}$ sub-units, then the α_2^A sub-units for the formation of Hb-*A* and Hb-A_2 could be derived from a common pool. It would then follow that an individual who made α_2 sub-units different from those found in Hb-*A* would not only show the corresponding variant of Hb-*A* but also of Hb-A_2. This has been found to be so. In the individual with Hb-*G* disease, who only makes α_2^G sub-units, no Hb-A_2 but a different minor component, Hb-G_2 ($\alpha_2^G\delta_2^{A_2}$), was found[4,5]. Both Hb-A_2 and Hb-G_2 were seen in two unrelated individuals carrying Hb-*A* as well as Hb-G_{α} (unpublished observations).

It also follows that if the α_2^A sub-units of both Hb-*A* and Hb-A_2 are derived from a common pool, then their formation is controlled at the same genetic locus.

The formation of the other series of Hb-A_2 variants which can occur without any concomitant abnormality of Hb-*A*, such as Hb-$A_2^{\prime}$ (ref. 2) and Hb-B_2 (ref. 3), indicates that there is a further, separate locus controlling the synthesis of Hb-A_2 and it is suggested that this locus, the δ locus, determines the formation of the $\delta_2^{A_2}$ sub-units. The genotype relevant to the formation of Hb-A_2 in a normal individual would then be α^A/α^A, $\delta^{A_2}/\delta^{A_2}$.

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Composition of Various Ribonucleic Acid Fractions from Micro-organisms of Different Deoxyribonucleic Acid Composition

The ratio of guanine plus cytosine to adenine plus thymine (GC/AT) in the deoxyribonucleic acid (DNA) of a given species of a micro-organism is constant, but the GC/AT ratio of different kinds of micro-organisms can vary by a factor of as much as five times[1]. The ratio of GC content to AU (uracil) content of cell ribonucleic acid (RNA) varies only slightly from one organism to another; but this ratio tends to be slightly higher in organisms the DNA ratio of which is high[2]. These facts raise a question as to whether all the RNA of a cell has the same composition or whether perhaps a small RNA sub-fraction has the same base ratios as its corresponding DNA (uracil being equivalent to thymine). Recent experiments have demonstrated an RNA sub-fraction in yeast which does have a composition almost identical to the corresponding DNA (ref. 3). The present work is concerned with analysing the nucleotide ratios in sub-fractions of the RNA from organisms with varying GC/AT ratios in the DNA.

The organisms chosen for this work were *Diplococcus pneumoniae*, in which GC is equal to 38 per cent of total DNA bases; *Escherichia coli*, GC of 50 per cent; and *Micrococcus lysodeikticus*, GC of 72 per cent (ref. 4 and Guild, W. R., personal communication). The organisms were grown in 'Trypticase-soy' medium (Balt. Biol.) at 37° C., with the exception of *D. pneumoniae*, grown in 'Bactotryptose' medium (Difco)[5]. The bacterial growth was collected by centrifugation, suspended in a 0·02 *M tris*(hydroxymethyl)aminomethane buffer containing 0·01 *M* magnesium chloride, and the cells ruptured by passage through a French pressure cell at 5,000 lb. pressure. The resulting suspension was cleared of cell debris by low-speed centrifugation followed by centrifugation at 100,000*g* for 5 min. Deoxyribonuclease was then added to break down DNA to relatively small polynucleotide units. It is impossible for DNA of this size-range to produce significant contamination of any of the final RNA fractions defined here. Three RNA fractions were experimentally defined as follows; a first pellet resulted from centrifuging the cell extracts for 2 hr. at 100,000*g* in a refrigerated Spinco model *L* centrifuge. This pellet should contain all microsomal material of 50*S* sedimentation constant and larger as well as most 30*S* microsomes[6]. A second pellet resulted from centrifuging the supernatant of the previous centrifugation for 5 hr. at 100,000*g*. This should contain mainly material sedimenting with sedimentation constants between 15*S* and 30*S*. For the third fraction, the supernatant of the second fraction was adjusted to *p*H 5 with acetic acid, the resulting precipitate collected by low-speed centrifugation, and redissolved in *p*H 7 buffer. This solution contains the soluble RNA of the cell[7]. Each of the nine fractions defined above was then extracted with water-saturated phenol twice, according to Kirby[8]. Relatively pure RNA was then precipitated by addition of two volumes of cold ethanol, collected by centrifugation, washed again in ethanol, and stored at −20° C. Approximately 10 mgm. of RNA from each fraction was hydrolysed in 1 *N* potassium hydroxide at 35° C. for 18 hr., the potassium ion being afterwards removed by neutralization with perchloric acid. This procedure degraded the RNA to a mixture of 2′- and 3′-nucleotides[9]. The ribonucleotides of the four main bases were separated by paper electrophoresis in a buffer at *p*H 3·6, according to the methods of Markham and Smith[10]. The paper strips containing the nucleotides were afterwards scanned with an ultra-violet lamp ('Mineralight *R*') to locate the separate nucleotide bands. Each band was then cut out and eluted overnight in phosphate buffer *p*H 7·5. The ultra-violet absorption spectrum for each nucleotide band was determined in the range 2350–2900 Å. Known mixtures of 2′-, 3′-ribonucleotides were run through the entire hydrolysis procedure in order to determine properly the amounts of each nucleotide present in the RNA hydrolysates. 7–13 electrophoretic runs were made on each fraction. At least two separate hydrolyses by potassium hydroxide of each microsomal RNA fraction occurred. No significant differences in nucleotide ratios between different hydrolyses of the same RNA fraction were observed.

Table 1. Nucleotide Composition of RNA Fractions. *C*, *G*, *U* and *A* refer to Cytidylic, Guanylic, Uridylic and Adenylic Acids respectively

		Large microsome RNA	Small microsome RNA	Soluble RNA
D. pneumoniae	*C*	19·2 ± 0·6	18·9 ± 0·5	22·9 ± 0·5
	G	31·1 ± 1·0	30·7 ± 0·7	29·7 ± 0·8
	U	24·0 ± 0·7	24·8 ± 0·5	25·0 ± 0·3
	A	25·4 ± 0·4	25·4 ± 0·6	22·2 ± 0·2
	C + *G*	50·3 ± 1·6	49·6 ± 1·2	52·6 ± 1·3
	U + *A*	49·4 ± 1·1	50·2 ± 1·1	47·2 ± 0·5
E. coli	*C*	20·1 ± 0·8	20·7 ± 0·3	24·7 ± 0·5
	G	32·4 ± 0·8	31·7 ± 0·7	32·0 ± 0·9
	U	22·6 ± 0·4	23·2 ± 0·5	22·5 ± 0·4
	A	24·7 ± 0·3	24·2 ± 0·4	20·5 ± 0·5
	C + *G*	52·5 ± 1·6	52·4 ± 1·0	56·7 ± 1·4
	U + *A*	47·3 ± 1·9	47·6 ± 0·9	43·0 ± 0·9
M. lysodeikticus	*C*	20·8 ± 0·4	22·1 ± 0·5	25·1 ± 0·5
	G	33·3 ± 0·8	31·5 ± 1·3	31·7 ± 0·8
	U	22·7 ± 0·7	24·1 ± 0·9	23·4 ± 0·5
	A	23·0 ± 0·5	22·2 ± 0·3	19·6 ± 0·5
	C + *G*	54·1 ± 1·2	53·6 ± 1·8	56·8 ± 1·3
	U + *A*	45·7 ± 1·2	46·3 ± 1·2	43·0 ± 1·0

The results are presented in Table 1. The values represent averages of all determinations on a given sample. Errors are presented as probable error. The base ratios for the first RNA fraction of *E. coli* (large microsomes) are the same as those given by Spahr and Tissières for *E. coli* 70*S* microsomes, except for the value of cytosine, which is significantly lower in the present instance[11].

The most obvious result in Table 1 is that none of these RNA fractions has a base ratio approaching that of cell DNA. However, the DNA composition of a given organism does seem to be reflected slightly in the composition of all the RNA fractions. In all three such fractions from each organism there is a statistically significant increase in cytosine and decrease in adenine as the GC content of cell DNA increases. In two of the three cases there is also a significant rise in guanine content, but the results do not give a clear indication of uracil changes as a function of GC content of DNA; a drop in uracil is suggested.

Generally, there is no statistically significant difference between the composition of RNA from small microsomes and that of RNA from larger ones for any given organism. The only exception to this is that in *M. lysodeikticus* cytosine represents a significantly higher per cent of total bases in small microsomes than in large ones. Spahr and Tissières found similarly that the fraction of cytosine in RNA

from 30*S* microsomes was significantly higher than that in 50*S* microsomal RNA in *E. coli*[11].

A difference in composition between soluble RNA and microsomal RNA exists. Soluble RNA is significantly higher in cytosine and lower in adenine than is microsomal RNA. However, there is no significant difference in the guanine and uracil composition of the microsomal and soluble RNA's.

In these experiments I have been unable to demonstrate a fraction of cell RNA that has a composition equal to that of its corresponding DNA (assuming uracil to be equivalent to thymine). However, as stated above, such a fraction has been reported for yeast. It seems a possibility then, that all the fractions in the present work are heterogeneous in that they contain a small amount of RNA which has base ratios equivalent to its corresponding DNA, thus producing slight variations in the average base ratios of each fraction in the direction of the base ratios of the corresponding DNA's.

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Total Cytochrome Oxidase Activity and its Relation to Basal and Maximal Metabolism

THE study of the values of the basal metabolic rate in mammals and its relation to body-weight has been the object of many papers and reviews since the middle of the nineteenth century. On the other hand, very few data are available concerning the upper limit of animal metabolism; only individual values are found in the literature concerning the maximal metabolism of some mammals and man. The incompleteness of the available data and their suitability for comparative purposes are connected with the difficulty in obtaining the state of maximal performance in animals. In addition, in many of the animals used, maximal oxygen consumption can be obtained only under simultaneous application of work and lowered temperatures, so that the working and thermoregulatory capacity of the animals are used as well. In these conditions, however, a rapid decrease of metabolism occurs as a result of cooling the animals, as I have already shown[1]; it is very difficult, therefore, to find out the period of greatest oxygen consumption. Nearly all the data in the literature seem to be affected by this error, and the results obtained are, therefore, probably lower than true maximal values.

I have looked for other possibilities for a more precise determination of maximal metabolism. It has been found that there exists a constant quantitative relationship among different oxidative enzymes and that the cytochrome oxidase activity readily becomes adapted to various conditions; this suggests that an excess of oxidative enzymes is not present in tissues. It would be expected, therefore, that the maximal possible oxygen consumption of animals and organs will correspond to the terminal oxidative enzyme, the cytochrome oxidase.

I have therefore determined the cytochrome oxidase activity of whole organisms at 37° C. manometrically[2], and the values of oxygen consumption thus obtained have been compared with the values of maximal working metabolism measured in living animals. Before homogenization the animals were depilated, the digestive tract removed and the carcase ground in a meat grinder.

The total cytochrome oxidase activity was determined in six species of rodents (bank vole, field vole, mouse, golden hamster, rat, guinea pig) of body-weight 19–700 gm. It was found that the total cytochrome oxidase activity is proportional to a power of the body-weight, the exponent being very near that found for basal metabolism, namely, 0·67 (Table 1). A similar relationship was also found in various organs and in the musculature of some other mammals[4].

Table 1. AVERAGE CYTOCHROME OXIDASE ACTIVITY IN VARIOUS MAMMALS

Species	Weight of animals without digestive tract (gm.)	Weight of dry substance (gm.)	Cyt. ox. activity (mm.³ oxygen/hr./mgm. dry substance)	Total cyt. ox. activity (ml. oxygen)	Month
Guinea pig	521·0	202·0	24·1 ± 6·4	4,870	V–VI
Rat	254·0	70·0	24·1 ± 1·7	1,690	III–VI
Golden hamster	64·0	16·8	62·6 ± 3·6	1,050	IX
Mouse	20·6	5·0	62·9 ± 6·7	316	III–IV
Bank vole	17·5	5·4	60·5 ± 8·1	327	IX–XI
Field vole	16·1	5·2	63·0 ± 8·0	327	X

The absolute values of the total cytochrome oxidase activity are found to be very nearly the same as the maximal metabolism of whole animals; the difference does not exceed ± 25 per cent (Table 2). Later experiments have shown that the values of cytochrome oxidase activity measured at 37° C. are not the true maximal values; maximal oxygen consumption is reached at other temperatures, which are different for different animals[5]; this factor may diminish the difference between the values of total cytochrome oxidase and maximum metabolism.

Table 2. COMPARISON OF MAXIMAL METABOLISM VALUES WITH VALUES OF AEROBIC METABOLIC CAPACITY IN VARIOUS MAMMALS

Species	Maximal metabolism (ml. oxygen/hr./gm.)	Cyt. ox. activity (ml. oxygen/hr./gm.)*	Difference (percentage of maximal metabolism)
Golden hamster	13·40	16,40	+ 22
Mouse	17·50	15·35	− 12
Field vole	16·10	20·30	+ 26
Bank vole	22·40	18·60	− 17

* Cytochrome oxidase activity was measured at 37° C. and referred to 1 gm. of body-weight without digestive tract.

A similar close correspondence between the values of the total cytochrome oxidase activity and maximum oxygen consumption during physical work has been recently found in an insect[6]. Thus this seems to indicate a more general relationship. The methods with which these two values were obtained are, however, so different that they should not be regarded as physiologically identical, and I suggest the term 'aerobic metabolic capacity' for the total activity of cytochrome oxidase, measured manometrically at the optimum temperature and expressed as oxygen consumption, while the values obtained with living animals should be referred to as 'maximal metabolism'.

It seems to me that the determination of the aerobic metabolic capacity may be of value, especially for comparative purposes, as it is readily found and is much more reproducible than the value of maximal metabolism.

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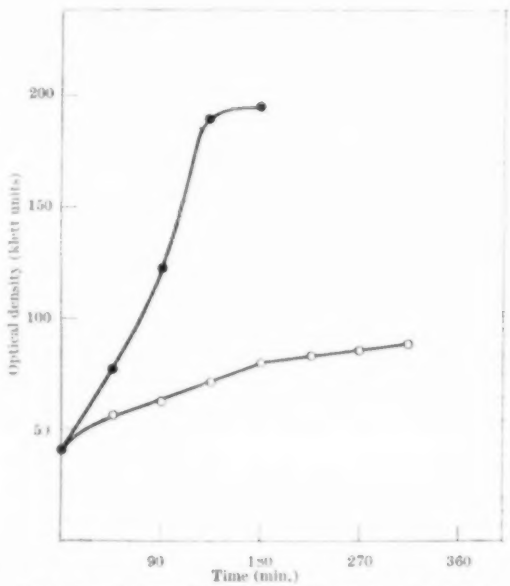


Fig. 1. Growth curve of strain *M*-39 *A*-23 growing in the presence of 20 μgm./ml. arginine with (○) and without (●) 200 μgm./ml. 2-thiouracil

A Requirement for 2-Thiouracil of 2-Thiouracil-grown *Escherichia coli* under Conditions of Ornithine Transcarbamylase Repression

Pyrimidine analogues may interfere with nucleic acid metabolism by inhibition of the conversion of the free pyrimidine bases to the corresponding nucleotides or by production of abnormal nucleic acids containing substituted pyrimidines. Recently it has been found that an analogue may also function by negative feed-back control and thus inhibit the formation of the normal metabolite[1,2].

This communication describes an additional effect of the uracil analogue 2-thiouracil which was observed under conditions of ornithine transcarbamylase repression. A mutant requiring ornithine, citrulline or arginine (*M*-39 *A*-23) derived from *Escherichia coli* strain *W* was used. 2-Thiouracil was added to cells of this mutant, in logarithmic phase, grown with aeration in minimal medium supplemented with glucose and arginine. As is shown in Fig. 1, a linear increase in optical density with time from 45 to 180 min. is observed. When cells grown for 45–135 min. in the presence of 2-thiouracil were plated on minimal medium supplemented with arginine, up to 90 per cent of the cells lost their ability to form colonies (Fig. 2).

However, when the 2-thiouracil-grown cells were plated on minimal medium containing 2-thiouracil, all the cells were capable of colony formation. It can be seen from Fig. 2 that after pre-incubation periods with 2-thiouracil exceeding 135 min., the proportion of the cell population capable of colony formation on minimal medium without 2-thiouracil increased. Eventually the same colony count was observed on minimal agar plates with or without 2-thiouracil. The transitory nature of the 2-thiouracil

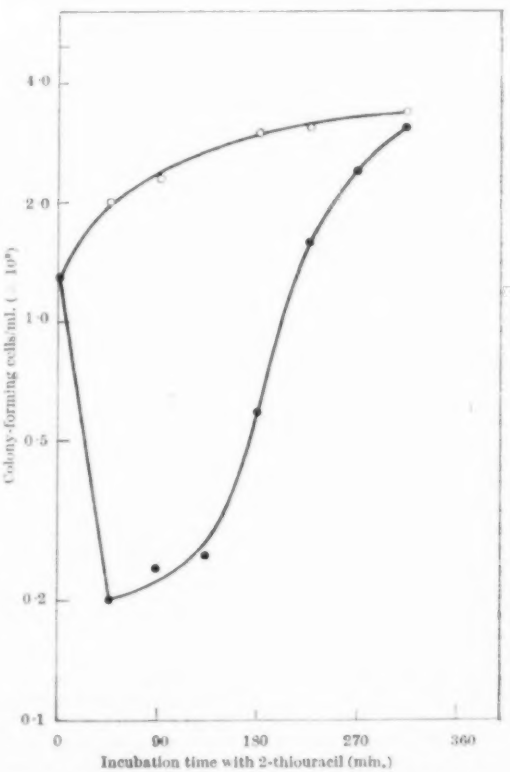


Fig. 2. Colony counts of strain *M*-39 *A*-23 preincubated with 20 μgm./ml. arginine and 200 μgm./ml. 2-thiouracil for the periods indicated, then plated on minimal agar plates with (○) and without (●) 50 μgm./ml. 2-thiouracil

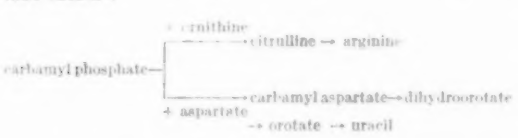
requirement was found to be due to changes in the level of arginine in the pre-incubation medium. Exhaustion of arginine relieved the cells from the 2-thiouracil requirement.

The 2-thiouracil requirement was also obtained when the mutant was grown with 2-thiouracil in the presence of citrulline. However, when the mutant was grown with 2-thiouracil in the presence of ornithine, inhibition of growth was less marked and neither loss of viability nor a 2-thiouracil requirement was observed when these cells were plated on to minimal medium.

Wild-type *E. coli W* cells are only slightly inhibited by 2-thiouracil. However, when arginine was added to the growth medium, 2-thiouracil exerted a marked inhibitory effect and also showed the 2-thiouracil requirement.

In all the experiments described, the 2-thiouracil requirement occurred when the synthesis of ornithine transcarbamylase, which catalyses the conversion of ornithine to citrulline, was repressed. This repression occurs in *E. coli W* and its mutant with arginine or citrulline but not with ornithine. In *E. coli B*, a non-repressible strain[3], no 2-thiouracil requirement was observed under the conditions described.

These results suggest a mechanism based on the metabolic relationship existing between arginine and uracil:



It has been suggested that these syntheses are to some extent competitive[4] and regulated by negative feed-back mechanisms[4,5].

Preliminary results show that 2-thiouracil mimics the feed-back action of uracil. Experiments are now in progress to elucidate the mechanism of the 2-thiouracil effect described.

We are indebted to Dr. B. D. Davis for strain *M*-39 *A*-23 used in this investigation.

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A Fatty Acid / Protein Complex in Human Hair

In an earlier publication[1] a new sensitive method for the detection of small amounts of damage to human hair was reported. The method involves counting the numbers of cuticular and cortical cells in the liquid after treating the hair under standard conditions with papain/bisulphite solution. When the ratio of cuticle cells to cortical cells is low, the hair is assumed to have been damaged in some way. Soxhlet extraction of the hair with ethanol increases the rate of breakdown, but ether, benzene and many other non-polar solvents do not affect the ratio. It was suggested that a protective substance soluble in alcohol but not in non-polar solvents exists in the hair which maintains it intact during papain digestion. This protective substance has now been isolated from ethanol extracts and identified as a fatty acid/protein complex.

Isolation by solvent fractionation was impracticable because the materials denatured at liquid/liquid interfaces. Silica fractionation by the method of Hanahan[2] was also unsatisfactory as the material was irreversibly adsorbed on the silica. Successful isolation was achieved by electrophoresis on polyurethane sponge in dilute acetic acid at *p*H 2·5. Under these conditions fatty acids and neutral fatty materials do not move, but the complex moves towards the negative electrode. Analysis of the isolated complex shows that it consists of 20–30 per cent fatty acid and 60–70 per cent protein, which yield substantial amounts of lysine but very little cystine. Methyl esters of the fatty acids are not volatile under normal GLC conditions, but the mass spectrometer indicates there is considerable variation between samples. Treatment of alcohol-extracted hair with an alcoholic solution of the complex reduces the rate of breakdown of hair to the normal level. This is not due to enzyme inactivation, since the degradation of casein by papain is not affected by the presence of the complex. The complex is positively charged in acid solutions and the rate of migration on paper electrophoresis decreases as the *p*H is made more alkaline until no movement is observed at *p*H 6·0. The complex then remains at the origin at *p*H values up to 9·5. This, combined with the high level of lysine, suggests that the fatty acid is combined through the amino-groups of the lysine so that the effective isoelectric point is in the range for normal proteins. In alkaline solution, negatively charged fatty acid residues are removed and this maintains the electrical neutrality of the protein.

I wish to thank Unilever, Ltd., for permission to publish this communication.

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PHYSIOLOGY

Distribution of Acetylcholine and Cholinesterase in the Heart of White Rats

The opinion has been advanced that acetylcholine acts in the heart not only as the mediator of the vagus nerve but also as the so-called local hormone in local extraneural regulation of heart activity and that in this last function it is closely associated with heart automation[1]. If this view is correct, it can be assumed that the most rapid turnover of acetylcholine will occur in those parts of the heart which possess the highest degree of automation. In order to verify the correctness of this assumption, experiments were carried out in which the distribution of acetylcholine and cholinesterase in different parts of white rat heart was examined.

White rats of either sex were used. The animals weighed 190–365 gm. On account of the small

amount of tissue available, two animals had to be used for each experiment when the content of acetylcholine was estimated and four animals when the activity of cholinesterase was assayed. The animals were killed by a blow on the head and decapitated. The heart was removed and sectioned as follows: the atria were separated from the ventricles and cut into three parts; the first part represented the region near the opening of the right superior vena cava into the right atrium, the second part the rest of the right atrium with the septum and the third part represented the left atrium; samples of suitable size were removed from the left and right ventricles. The content of acetylcholine bound in heart tissue was estimated by Rothschuh's method[2], employing modifications proposed by Vlk[3]. The activity of cholinesterase was assayed on the basis of the rate of degradation of acetylcholine during incubation of the homogenate of the corresponding part of the heart in a medium containing 200 μgm. acetylcholine chloride per ml. for 30 min. at 38° C. The concentration of acetylcholine was estimated by a chemical method based on the transfer of acetylcholine to the ferric complex of acetohydroxamic acid. Intensity of the red colour was measured with a Coleman spectrophotometer at 540 mμ.

Table 1. Contents of Acetylcholine (ACh) and Activities of Cholinesterase (ChE) in Different Parts of White Rat Heart
The figures in brackets represent the number of experiments

Part of the heart	ACh content ± S.D.	Activity of ChE ± S.D.
The region near the opening of the right superior vena cava into the right atrium	7·07 ± 1·15 (9)	129 ± 3·74 (6)
The rest of the right atrium with septum	5·91 ± 0·94 (9)	114 ± 2·35 (5)
Left atrium	2·16 ± 0·56 (9)	103 ± 2·06 (6)
Right ventricle	—	79 ± 4·86 (6)
Left ventricle	—	71 ± 2·65 (6)

The results are summarized in Table 1. The content of acetylcholine is expressed as μgm./gm. fresh tissue and the activity of cholinesterase as μgm. acetylcholine chloride decomposed by 1 ml. mixture. The content of acetylcholine was determined in the atria only as its distribution in heart ventricles of rats had been known from the paper of Rothschuh[4]. The ventricles are known to contain much less acetylcholine than the atria, the right ventricle having a higher content of acetylcholine than the left one. The highest content of acetylcholine and activity of cholinesterase were detected in the region near the opening of the superior vena cava, whence the levels decrease in the direction of listing the individual parts of the heart in Table 1. The above-mentioned gradient of distribution of acetylcholine and cholinesterase was found in all cases investigated here. The content of acetylcholine decreases much more markedly than the activity of cholinesterase, as shown in Fig. 1, in which the content of acetylcholine and the activity of cholinesterase are expressed as percentage of the basic value which was identified with the value from the opening of the superior vena cava. The right-hand side of Fig. 1 represents the distribution of cholinesterase, the left-hand side the distribution of acetylcholine; the data of the content of acetylcholine in the right and left ventricles were computed from Rothschuh's results[4].

It follows from the results that the highest content of acetylcholine and the highest activity of cholinesterase are to be found in that part of the heart where the rhythmic impulses regulating the automatic activity of the heart are normally generated. This finding is in agreement with the results of Mazel and Holland[5], who found that the most rapid turnover of acetylcholine in poikilothermic animals occurs in the sinus venosus, that is, in the part of the heart which possesses highest automation as assessed from the frequency of contractions of isolated parts. Our results support the view that acetylcholine turnover is of considerable significance in processes which represent the basis of automatic activity of the heart. A detailed report will be published in *Physiologia bohemoslovenica*.

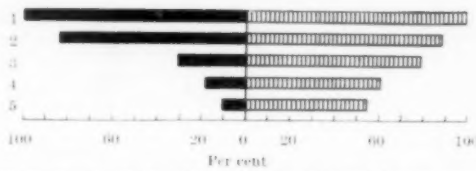

Fig. 1. The distribution of acetylcholine (black) and cholinesterase (shaded) in different parts of white rat heart. 1, Values for the region near the opening of the right superior vena cava in the right atrium; 2, the rest of the right atrium with septum; 3, the left atrium; 4, the right ventricle; 5, the left ventricle

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Pharmacological Specificities of Neurones in an Elementary Central Nervous System

Recent pharmacological investigations by us[1] on the central nervous system of the mollusc *Aplysia depilans* revealed acetylcholine as a possible synaptic transmitter of inhibition. The evidence was obtained by electrophysiological methods; different cells in the abdominal ganglion of this animal were impaled by glass microelectrodes according to previously described techniques[2] and their reactions observed in the presence of different drugs. It was thus shown that externally applied acetylcholine in concentrations up to 10^{-12} hyperpolarizes the membrane and mimics the inhibitory postsynaptic potentials in cells having inhibitory input (conventionally designated as *H*-cells), whereas other cells having only excitatory input (*D*-cells) are depolarized by acetylcholine (Fig. 1*A*). In both cases the impedance of the membrane drops to a low level. The action of acetylcholine on *H*-cells is reversed when the level of polarization of the membrane is increased by artificially applied current. The reversal-level for acetylcholine potentials and inhibitory postsynaptic potentials have equal values, suggesting an identical selective permeability variations of the membrane. In *D*-cells the equilibrium-level is close to the zero membrane potential, indicating a different and non-selective permeability change. Local electrophoretical injections of acetylcholine disclosed a type of response which is identical in synaptic regions as well as in proximal extrasynaptic

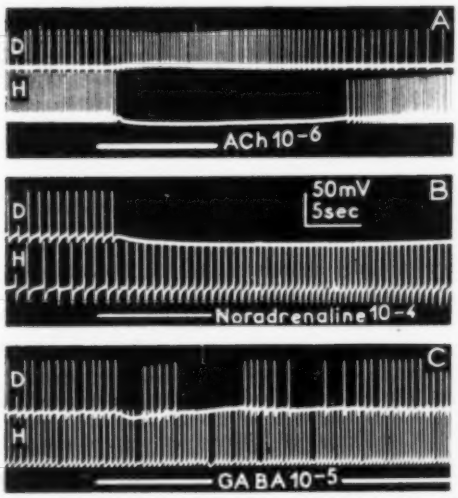

Fig. 1. Action of different drugs (horizontal line) on the spike activity of spontaneous *D* and *H Aplysia* ganglion cells. Simultaneous intracellular recordings from two neurones

membranes; but the axonal synaptic fields are more sensitive to acetylcholine than the somatic membrane where, as usual in molluscs, there are no synaptic terminals[2]. D-Tubocurarine and atropine in external solutions reduce the inhibitory postsynaptic potentials as well as the action of acetylcholine, whereas eserine first lengthens the inhibitory effect and then reduces the size of inhibitory postsynaptic potentials by inactivating the postsynaptic membrane; excitatory postsynaptic potentials in *H*-cells are not affected. Consequently, we concluded that the inhibitory synapse in the *Aplysia* central nervous system is cholinergic.

Very striking were the opposite reactions to acetylcholine of contiguous cells; and it was interesting to see that this specific difference of the two types of neurones appears also with other types of drugs usually considered as having a synaptic action. However, the type of response is different from acetylcholine action. Noradrenaline in solutions up to 10^{-4}, in contrast to acetylcholine, hyperpolarizes

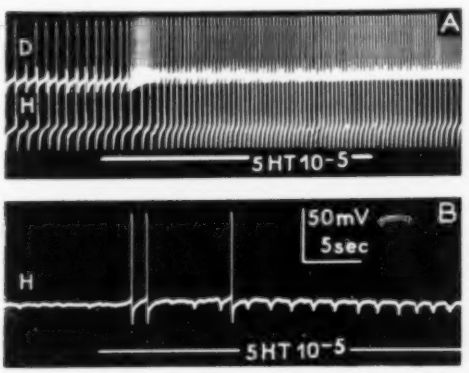

Fig. 2. *A*, Simultaneous intracellular recordings from two spontaneous *Aplysia* cells of different type on application of 5-hydroxytryptamine. *B*, The primary excitatory effect of 5HT on an *H*-cell is masked by inhibitory postsynaptic potentials due to a simultaneous activation by the drug of inhibitory interneurones

and inhibits the *D*-neurones and activates the *H* type (Fig. 1*B*). Adrenaline has the same effect, but is about five times less active than noradrenaline.

γ-Amino-butyric acid (GABA), the participation in inhibitory processes of which was recently discussed[4], usually has a depolarizing and excitatory effect upon the *H*-cells, whereas the *D*-cells, devoid of inhibitory input, are always hyperpolarized and inhibited (Fig. 1*C*). In some cases the *H*-cell is inhibited by GABA; but this action is not similar to the characteristic transient hyperpolarization provoked by this drug in *D*-cells.

5-Hydroxytryptamine (5HT) excites the two types *H* and *D*, but its effect is more than ten times more intense on *D*-cells (Fig. 2*A*). 5HT is apparently present in the molluscan nervous system[5], and its participation in synaptic transmission has also been considered[6].

When the effect of drugs is studied by perfusing the whole ganglion, the true pattern of response of the membrane to the drug may be changed by the interference of interneurones, which are also affected by the drug. For example, 5HT, the primary action of which is excitatory, can indirectly inhibit an *H*-cell by exciting at the same time an inhibitory interneurone, thus producing inhibitory postsynaptic potentials in the impaled cell (Fig. 2*B*). This may be avoided by injecting the drug locally; but the perfusion has the advantage of giving additional information about the action of the drug on the interneurone, the activity of which is reproduced in the synaptic pattern recorded in the cell by intracellular electrode. This method enabled us to establish that the inhibitory internuncial neurones, responsible for the inhibitory input on *H*-cells, are of the *D* type.

Conclusions from this work may be summarized as follows:

(1) Two types (*H* and *D*) of neurones with different and specific pharmacological properties are present in the central nervous system of *Aplysia*. These specificities are demonstrated by the response of the *H*- and *D*-cell membranes to acetylcholine, noradrenaline, adrenaline, 5HT and GABA.

(2) The type of pharmacological response is the same on the synaptic and extrasynaptic regions close to the cell body.

(3) The pharmacological pattern of the inhibitory interneurone corresponds to the *D*-type.

(4) These differences in pharmacological specificities of neurones with apparently no special localization in an elementary central nervous system show the difficulties presented by pharmacological studies of neuronal groups and the advantage of concentrating the pharmacological analytical research as much as possible on elementary structures.

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Apparent Absence of Amines in Cerebrospinal Fluid of Phenylketonurics

The mechanism by which mental defect is produced in phenylketonuria is unknown. No correlation has been found in patients having this disorder between the degree of mental defect and blood-levels of phenylalanine or phenylpyruvate, or urinary excretion of phenylalanine, phenyllactate, phenylpyruvate or *o*-hydroxyphenylacetate[1]. The possible implication of biologically active amines has been examined in several papers. Mitoma *et al.*[2] administered *o*-tyrosine and *m*-tyrosine to experimental animals and observed conversion to the corresponding amines in brain, with attendant central nervous system stimulation and convulsions. Association of the mental defect in phenylketonuria with an excessive production of *o*-tyramine was suggested. It also seems possible that overproduction of phenylethylamine may be responsible for the disturbance in cerebral metabolism. Jepson *et al.*[3] have recently shown that administration of a monoamine oxidase inhibitor to phenylketonuric individuals results in an increase much greater than normal in the urinary excretion of phenylethylamine, but not of *o*-tyramine. The mental defect in phenylketonuria may also be due to an underproduction of amines vital to normal brain function. Pare *et al.*[4] have reported low serum serotonin-levels and decreased urinary excretion of 5-hydroxyindoleacetic acid in phenylketonuria. They suggest that one or more aromatic acid metabolites of phenylalanine inhibit 5-hydroxytryptophan decarboxylase, the enzyme responsible for the production of serotonin.

It was felt that the demonstration of the presence or absence of biologically active amines in cerebrospinal fluid might give clues to the mechanism of the mental defect in phenylketonuria. Because cerebrospinal fluid is formed in the ventricles and bathes the brain, it may be in a better position than other body fluids to reflect the biochemical changes occurring in the brain in disease. In the recently discovered disorder argininosuccinicaciduria[5], the concentration of argininosuccinic acid has been found to be greater in cerebrospinal fluid than in plasma, and may reflect a derangement in cerebral metabolism.

In the present work, 4 phenylketonuric children and 4 control children of similar ages having mongolism were given orally a potent monoamine oxidase inhibitor, β-phenyl*iso*propylhydrazine ('Catron', *JB*-516), in a dosage of 9–12 mgm. once daily for 12–14 days. Before and again after 12–14 days of monoamine oxidase blockade, 10 ml. of cerebrospinal fluid was obtained from each patient by lumbar puncture. Cerebrospinal fluid was stored at − 20° C. until used. None of the patients exhibited any consistent change in behaviour while receiving 'Catron', other than that expected incident to the discomfort of removing cerebrospinal fluid.

Specimens of cerebrospinal fluid were deproteinized by ultrafiltration at 5° C. for 24–36 hr. Amines were absorbed on the resin 'Amberlite *CG*-50', type 2 (H^+ form) according to the method of Awapara *et al.*[6]. Each filtrate of cerebrospinal fluid was shaken for 1 hr. with 1 gm. of resin on a mechanical shaker, the resin was washed with water in a column, and the bases were then eluted with 4 *N* acetic acid. The eluate was lyophilized, and the residue was dissolved in 0·5 ml. of 10 per cent aqueous 2-propanol.

The concentrates of cerebrospinal fluid were chromatographed one-dimensionally on Whatman No. 1 paper in butanol/acetic acid/water (12 : 3 : 5). The equivalent of 1 ml. of original cerebrospinal fluid was applied to each chromatogram. Individual chromatograms were prepared from each specimen for development with ninhydrin, diazotized *p*-nitroaniline, and *p*-dimethylaminocinnamaldehyde. As little as 0·05 μgm. of serotonin, 0·25 μgm. of *o*-tyramine and 0·25 μgm. of phenylethylamine could be detected readily. Graded amounts of these authentic amines were chromatographed simultaneously on the same sheet with each specimen of cerebrospinal fluid.

No amines were detected in 1 ml. of cerebrospinal fluid from each of the 4 phenylketonuric and 4 mongoloid patients, either before or during monoamine oxidase blockade. The unused portions of concentrates of cerebrospinal fluid obtained during monoamine oxidase blockade were then pooled, and most of the salts and basic amino-acids were removed by precipitation with ethanol and acetone according to the technique of Rodnight[7]. Again, no amines were detected on chromatograms prepared from 10 ml. of pooled phenylketonuric or pooled mongoloid cerebrospinal fluid.

The efficiency of the recovery procedure for amines in cerebrospinal fluid and the possibility that amines might be destroyed during deproteinization by monoamine oxidase naturally present in the cerebrospinal fluid were checked by adding authentic amines to cerebrospinal fluid. 2 μgm. of serotonin and 10 μgm. of phenylethylamine per ml. were added to cerebrospinal fluid obtained from phenylketonuric and mongoloid patients prior to monoamine oxidase blockade. The cerebrospinal fluid specimens were incubated for 4 hr. at 37° C. to promote possible enzymatic action, and then were deproteinized by ultrafiltration for 36 hr. at 5° C. The filtrates were processed and chromatographed as previously described. Recoveries of added serotonin and phenylethylamine were about 75 per cent.

The results show that cerebrospinal fluid of each phenylketonuric patient during monoamine oxidase blockade contained less than 0·05 μgm. of serotonin and less than 0·25 μgm. of phenylethylamine and *o*-tyramine per ml., and that pooled phenylketonuric cerebrospinal fluid contained less than 0·005 and 0·025 μgm. per ml. respectively of these amines.

The failure to detect amines in phenylketonuric and mongoloid cerebrospinal fluid during monoamine oxidase blockade may be due to insufficient sensitivity of the technique used. Published reports suggest that the concentration of amines in cerebrospinal fluid is very low, if indeed they are present at all. Sachs[8], using a biological assay method, found serotonin in cerebrospinal fluid of some patients with head injuries and brain tumours. It is possible, however, that this serotonin may have been derived from bleeding into the subarachnoid space. Weil-Malherbe and Liddell[9] determined epinephrine and norepinephrine fluorimetrically in cerebrospinal fluid, and found these amines present in average concentrations of 0·9 and 2·8 μgm./l. respectively. The possibility that, in the present experiment, amines originally present in the cerebrospinal fluid in low concentration were destroyed enzymatically has not been excluded, but this seems unlikely since the patients were given a potent monoamine oxidase inhibitor, and in view of the recovery of added authentic amines after incubation of cerebrospinal fluid.

It is likely that many intracellular biochemical alterations in the brain are not reflected in the cerebrospinal fluid. For example, γ-aminobutyric acid, present in relatively large amounts in the brain and the retina but not elsewhere in the body, is not normally found in cerebrospinal fluid. A failure to find amines in cerebrospinal fluid, even during monoamine oxidase blockade, may result simply from inability of these substances to penetrate from the brain or blood into the cerebrospinal fluid. Thus the results of the present work do not exclude the possibility that the mental defect in phenylketonuria may be related to an underproduction of serotonin, or an over-production of phenylethylamine or *o*-tyramine.

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Dynamics of Renal Proximal Tubular Secretion

A NUMBER of exogenous substances such as penicillin, 'Diodrast' and *p*-aminohippuric acid (PAH) are secreted in the proximal tubules. Nothing definitely is known about the mechanism of uptake of these substances in the tubular cells and further transport into the tubular lumen[1]. It is likely that enzymatic reactions are involved so that PAH reacts with an enzyme (carrier) in the cell membrane since the kidney cells seem to be impermeable to it. The concentration of PAH therefore approaches zero in the vicinity of the cell. However, it must traverse the wall of the capillary and the interstitial water before reaching the tubular cell. This probably takes place as diffusion along a concentration gradient. The concentration of PAH in the capillary plasma will therefore never be zero.

It is, however, not reasonable to explain in this way extraction of PAH (E) as low as 0·90 or lower at low plasma concentrations since similar extractions have been found for PAH and 'Diodrast' although these substances have very different diffusion coefficients[2]. When the flow of blood through the kidney is increased at unchanged arterial haematocrit, the extraction of PAH is considerably reduced (ref. 3 and unpublished work).

When blood with a low plasma concentration of PAH (c_0) reaches the glomeruli, fluid is filtered off, whereas the plasma concentration remains essentially unchanged. During the passage of the postglomerular capillaries the PAH concentration is reduced to $c_0(1 - E)$. The total amount removed and secreted into the tubular fluid is the sum of the amounts abstracted at all levels of the capillaries with decreasing concentration of plasma.

It is well known that the reaction velocity of enzymatic reactions, in this case the reaction which limits the transport-rate for PAH from interstitial fluid into tubular fluid, depends on the concentration of the substrate. The reaction velocity is low at low concentrations and increases to a maximum (V) which is uninfluenced by further increase in the concentration of PAH (c) delivered to the tubular cells. The relationship between reaction velocity and concentration of substrate is expressed in Michaelis's equation[4]:

$$v = Vc/(c + K_m) \qquad (1)$$

K_m is the Michaelis constant (the concentration of substrate at which the reaction proceeds at half the maximal velocity) and v is the amount of PAH abstracted from the capillaries per unit length and unit time. Since the concentration of PAH is decreasing during the passage of the capillary, it follows that:

$$v = -\mathrm{d}c/\mathrm{d}t \qquad (2)$$

where t is the time of passage through the capillary.

By combination of these two equations and integration for the time t between the limits for PAH concentration c_0 and $c_0(1 - E)$:

$$E + \ln(1/1 - E)K_m/c_0 = Vt/c_0 \qquad (3)$$

The rate of flow of plasma through the capillaries is inversely proportional to the passage time when the volume of the capillaries remains constant. The equation may therefore be rewritten:

$$E + K_m \ln(1/1 - E)/c_0 = K_0 f \qquad (4)$$

where K_0 is a constant and f is the flow-rate.

Maximal extraction values for PAH are obtained when its concentration is low (lower than K_m). The ratio K_m/c_0 is therefore larger than unity.

Fig. 1 shows that the extraction of PAH is reduced when the renal plasma flow-rate through the postglomerular capillaries is increased. The relationship between E and percentage increase of flow of plasma is in good accordance with experimental findings (unpublished). The basis for Fig. 1 is the assumption that the extraction is 0·8 at a renal plasma-flow of 200 ml./min. It is evident from the figure that the values for extraction of PAH at a given flow-rate are nearly identical whether the arterial plasma concentration for PAH is twice (filled circles) or ten times (open circles) smaller than K_m. This deduction is also in accordance with experimental findings.

This hypothesis explains why the extraction of PAH may be reduced without a similar reduction in Tm for PAH. At high plasma concentrations the amount removed will not vary with blood-flow. This can be shown by integrating the Michaelis equation with respect to capillary volume. The result is:

$$T - fK_m \ln(1 - T/fc_0) = K_1 \qquad (5)$$

where T is the total amount secreted per minute and K_1 is a constant. When the load of PAH ($fc_0 = L$) delivered to the tubular cells is large compared with the amount secreted, the second term in equation (5) vanishes, and T reaches its maximal value, usually called Tm. In titration curves for PAH the relation-

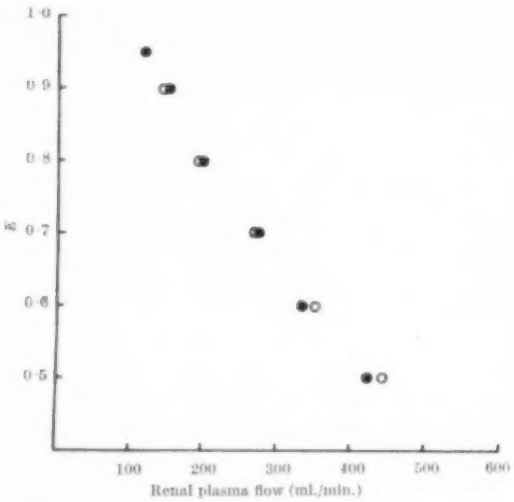

Fig. 1. Expected extraction of PAH at various rates of flow of plasma. ●, when $K_m/c_0 = 2$; ○, when $K_m/c_0 = 10$

ship between T/Tm and L/Tm is shown. The equation (5) may therefore be rewritten:

$$T/Tm - K_s \log(1 - (T/T_m/L/T_m)) = 1 \qquad (6)$$

where K_s is a constant when plasma flow is constant.

Fig. 2 shows the results for PAH-titration of a 53-year-old normal man[5], and the stippled curve is the titration curve for PAH as interpreted by Smith[6].

The other curve is plotted on the basis of equation (6), assuming $T/Tm = 0{\cdot}75$ and $L/Tm = 1$ as reference point. The shape of the curve obviously depends on this choice, and curves which fit the experimental data better may be found. According to equation (6) the tubular transport system is 90 per cent saturated when the load is slightly more than twice Tm, but 95 per cent saturation requires a load more than eight times larger than Tm. Tm is never reached, but only approached. As apparent from Fig. 2, Smith's and my estimates of Tm are different. The common assumption that there is no splay in the titration curve of an individual nephron obviously has to be reconsidered.

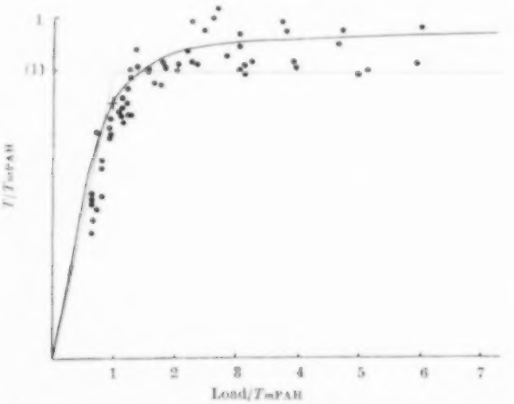

Fig. 2. PAH titration curve redrawn after H. Smith (ref. 6, 166). Solid line shows titration curve if Michaelis's equation is followed

A similar reasoning may be used for reabsorptive processes with a maximal reabsorptive capacity, but is more complicated since the decrease in concentration of the substrate during the passage of the proximal tubules is not only a function of the rate of reabsorption of the substrate but also a function of the considerable rate of water abstraction.

The model proposed suggests that the rate-limiting process for the transport of PAH follows Michaelis equation. This process is not necessarily localized in the cell membrane towards the tissue side, but evidently is a function of the substrate concentration in the interstitial fluid. The maximal rate of transport may therefore depend on the concentration of enzyme for the rate-limiting reaction. Competitive inhibition of transport processes may be interpreted along these lines. By means of titration curves for chemical analogues the constants V and Km in Michaelis's equation may be evaluated. The rate-limiting process may, however, not be the same for transport of different analogues.

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Minimum Rates of Flow in Therapy with Sulphonamides

Recent work on the kinetics of the acetylation of sulphisoxazole[1] and sulphamethylthiadiazole[2] in human beings indicate that excretion of acetylated drug is the terminal step in a two-step consecutive first-order process the first step of which is acetylation. This kinetic model was tested for ability to describe the metabolism and excretion of sulphathiazole taken by normal adult humans under a standard test procedure[1]. When 0·5-gm. doses were taken, excretion of acetylated drug was well described by the appropriate mathematical expression[1,2]. However, when one subject took a 1·0-gm. dose, it was not possible to describe the excretion of acetylated sulphathiazole by the same expression. The test was repeated with the same subject about two weeks later, and a water intake of about 500 ml./hr. maintained during the first 8 hr. of the test. This time excretion of the acetylated drug was well described by the expression. Using the rate constants obtained in the second test to calculate maximum excretion-rate of acetylated sulphathiazole by this subject from a 1·0-gm. dose, and comparison of this rate with the average urine flow-rate during the expected time of occurrence of the maximum during the first test, indicated that the solubility of acetylated sulphathiazole was exceeded at the average urine *p*H. It seemed reasonable to believe that crystalluria had occurred during the first test with a 1·0-gm. dose which would prevent description of excretion by the expression previously found to hold when a smaller dose was taken. There was no evidence of haematuria on casual gross examin-

ation of the urine specimens obtained in the first test with a 1·0-gm. dose.

The fact that the excretion of at least three acetylated sulphonamides[1-3] can be described in terms of several rate constants allows the following generalization to be made concerning minimum rate of flow of urine needed in therapy with these sulphonamides in order to prevent crystalluria.

Urine concentration of acetylated drug is given by :

$$Cu = \frac{dSae}{dt} \Big/ \frac{dU}{dt} \qquad (1)$$

where Cu is the concentration in mgm./ml., $dSae/dt$ excretion-rate of acetylated drug in mgm./hr. and dU/dt average rate of flow of urine in ml./hr. It is usual in therapy to give an initial loading dose of drug, followed by maintenance doses at regularly spaced intervals. This procedure establishes blood-concentration and body-level at a nearly constant value. Excretion-rate of acetylated drug is given by :

$$\frac{dSae}{dt} = k_2 Sa \qquad (2)$$

where k_2 is the first-order rate constant for excretion of acetylated drug in reciprocal hours and Sa is the amount of acetylated drug in the body at any time in mgm. The rate of change of acetylated drug in the body with time is :

$$\frac{dSa}{dt} = k_1 g - k_2 Sa \qquad (3)$$

where k_1 is the first-order rate constant for acetylation in reciprocal hours, and g is the constant amount in the body in mgm. For simplicity in mathematical treatment, it is assumed that the dose is instantaneously absorbed and equilibrium in body fluid is immediately obtained.

Equation 3 may be integrated and constant evaluated at zero time to obtain :

$$Sa = \frac{k_1 g}{k_2}(1 - \exp[-k_2 t]) \qquad (4)$$

Equation 4 reduces to the following at a time infinite in terms of the experiment :

$$Sa = \frac{k_1 g}{k_2} \qquad (5)$$

It can be calculated on the basis of data available for the mean value of k_2 for sulphisoxazole[1] that equation 4 is within 95 per cent of the value given by equation 5 in 40 hr.; with sulphamethylthiadiazole[2] in 4 hr., and with sulphathiazole (unpublished work) in about 8 hr. Substituting equation 5 in equation 2 gives :

$$\frac{dSae}{dt} = k_1 g \qquad (6)$$

Substituting equation 6 in equation 1 and rearranging gives equation 7 :

$$\frac{dU}{dt} = \frac{k_1 g}{Cu} \qquad (7)$$

If Cu in equation 7 is taken as the solubility of the acetylated sulphonamide at a given urine pH, then dU/dt becomes the minimum rate of flow of urine needed to prevent the occurrence of crystalluria.

Some calculations made with equation 7 are listed in Table 1. Solubility was calculated as a function of urine pH by the procedure of Krebs and Speakman[3] for sulphathiazole. Values for solubility of acetylated sulphisoxazole and acetylated sulphamethylthiadiazole at the several pH's were obtained from published values[4]. The mean value of k_1 used in each case was obtained from the work previously mentioned[1-3]. The value of g was taken as 1 gm. and, from equation 7, flow-rate is directly proportional to this quantity.

Table 1. Minimum Urine-rates of Flow (ml./hr.)

Urine pH	Sulphisoxazole	Sulphamethylthiadiazole	Sulphathiazole
5·0	190	90	420
5·5	60	60	400
6·0	20	40	370
6·5	10	20	280
7·0	5	10	170

Calculation of minimum values of rate of flow assumes no supersaturation of urine can occur, and that precipitation is immediate when solubility is exceeded.

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HÆMATOLOGY

Reduced Fibrinolytic Activity of Atherosclerotic Sera caused by an Increase in Low-density Lipoproteins in Blood

Recent work from several laboratories indicates abnormalities in bloods of atherosclerotic patients characterized by high cholesterol-level, elevation of cholesterol : phospholipid ratio and elevated low-density lipoproteins[1-3]. These abnormalities are reflected in a remarkably poor fibrinolytic activity of these bloods[1]. The work reported here was carried out in an attempt to find out the cause of low fibrinolytic activity of such bloods (collected from patients with advanced atherosclerosis), and to determine the nature of the material responsible for the inhibition. It is also hoped that such studies will enable us to find out the cause of frequent coronary deaths among older people after they have had fatty evening meals. The present work was based on analyses of blood specimens obtained from patients having a history of myocardial infarction, in the belief that these patients had developed atherosclerosis.

Blood samples collected from normal individuals (without known vascular or cardiac disease) between 30 and 40 years of age and from those with a history of coronary infarction were tested for fibrinolytic activity. The ability to dissolve a fibrin clot was used to measure the fibrinolytic activity of these blood sera. To each specimen an equal volume of highly purified fibrinogen[5] was added, mixed well and then thrombin was added to the mixture to produce clotting. The concentration of fibrinogen in the final solution was 0·2 per cent. Fibrinolytic activity was also measured in some cases after activation of the serum with streptokinase[6]. In general, the fibrinolytic activity of normal serum has always been found to be

Table 1. Fibrinolytic activity of Sera

Normals			Atherosclerotics		
No.	Age	Percentage of clot lysis in 24 hr.	No.	Age	Percentage of clot lysis in 24 hr.
1	32	100	1	65	60
2	36	85	2	58	70
3	31	92	3	62	65
4	39	80	4	72	60
5	35	86	5	61	70
6	38	100	6	57	65
7	33	95	7	64	58
8	32	95	8	66	75
9	38	100	9	62	70
10	37	82	10	67	64

30–35 per cent higher than the corresponding values for sera collected from atherosclerotic patients (Table 1).

Chylomicra and low-density lipoproteins were removed from the sera with a Spinco model *L* preparative ultracentrifuge according to the method developed by Havel *et al.*[7].

The removal of chylomicra and low-density lipoproteins from the blood of atherosclerotic patients results in an increase in fibrinolytic activity (Table 2). The subsequent removal of α-lipoproteins from these blood samples does not alter their fibrinolytic activities. The removal of low-density lipoproteins thus renders these blood samples indistinguishable from normal bloods which have also been subjected to similar treatment.

Table 2. Fibrinolytic Activity of Sera before and after Treatment

Normals				Atherosclerotics			
No.	Age	Percentage of clot lysis in 16 hr.		No.	Age	Percentage of clot lysis in 16 hr.	
		before treatment	after treatment*			before treatment	after treatment*
1	32	70	100	1	65	45	95
2	36	60	95	2	58	50	100
3	31	65	90	3	62	48	100
4	39	75	100	4	72	42	95
5	35	60	86	5	61	46	95
6	38	80	100	6	57	45	88
7	33	75	100	7	64	40	90
8	32	75	100	8	66	38	90

* Serum was either treated with chloroform/methanol mixture or subjected to the method of Havel *et al.* in order to remove chylomicra and low-density lipoproteins.

Repeated treatments (5–6 extractions) of normal serum or serum obtained from atherosclerotic patients' blood with chloroform–methanol mixture (1 : 1 by volume), which removes chiefly the low-density lipoproteins, tends to raise the fibrinolytic activity of the atherosclerotic patients' blood to the value of the normal blood after similar treatments, although originally the fibrinolytic activities of those samples had been different (Table 2). These findings are in good agreement with those reported by Greig and Runde some years ago[4]. Similar treatments of the plasma with petroleum ether (b.p. 40–60° C.), which renders the plasma unclottable by Russell's viper venom and calcium[8,9], fail to alter the fibrinolytic activity of these blood samples. The poor fibrinolytic activity of the circulating blood can thus be attributed to the presence of low-density lipoproteins rather than any free phosphatides. Another point of interest is the fact that phospholipids extracted from the serum by the use of a chloroform–methanol mixture cannot inhibit fibrinolysis, at least not at the physiological concentration-level, since streptokinase-activated plasminogen (streptokinase and human serum) requires almost as much time to dissolve a fibrin clot in the presence of phospholipids as in the absence of this material.

Since 1940, it has been known that blood, after repeated treatments with chloroform, becomes fibrinolytic; but it is not known what factor or factors (that can be removed by chloroform–methanol mixture) act as inhibitors of the fibrinolytic system of the circulating blood. One possible explanation might be that they form some type of inert complex with either plasmin or plasminogen, thereby preventing the former from acting on its substrate (fibrin clot) or the latter (plasminogen) from being spontaneously converted to plasmin. The fact that chloroform–methanol mixture can remove the factor or factors, acting as inhibitors in the circulating blood, implies their lipid nature. It is assumed that spontaneous conversion of plasminogen to plasmin is taking place all the time, although to a very limited extent; the reason why there is no clot-lysis under these conditions is perhaps due to the presence of an inhibitor (antiplasmin), acting against plasmin. If this explanation is correct then chloroform–methanol mixture actually removes this inhibitor from the blood; the fibrinolytic enzyme thus set free acts on fibrin clot (Fig. 1). The fact that serum-treated streptokinase exhibits much higher clot-dissolving activity than the chloroform–methanol-treated serum (Table 3), and also the fact that streptokinase cannot enhance fibrinolytic activity in bovine serum suggest that it must be acting in an entirely different way. The question is what it does then?

Streptokinase, as is known, combines with a pro-activator present in blood to form an activator which then converts plasminogen to plasmin. The activator has all the properties of a proteolytic enzyme[10]; and it is known that the conversion of plasminogen to plasmin can also be induced by trypsin or other mould enzymes[11]. Streptokinase has no proteolytic or esterase activity of its own; most probably it removes some specific inhibitor (anti-activator) from the circulating blood thereby facilitating the conversion of plasminogen to plasmin by the activator thus set free. In this scheme the consideration of the hypothetical pro-activator is superfluous. The reason why bovine serum, after treatment with streptokinase, does not acquire any fibrinolytic activity might be due to the absence of the activator in such serum.

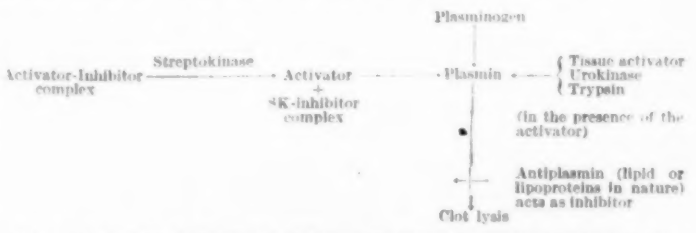

Fig. 1. Mechanism of action of streptokinase and chloroform/methanol mixture in the generation of fibrinolytic activity in blood.
Streptokinase removes the factor which inhibits the activator, whereas chloroform/methanol mixture removes the antiplasmin. Removal of low-density lipoproteins from serum is the removal of the antiplasmin

Table 3. Fibrinolytic Activity of Sera after Activation with Streptokinase

Normal group			Atherosclerotic group		
No.	Age	Time for clot lysis	No.	Age	Time for clot lysis
1	32	4m. 20s.	1	65	4m. 35s.
2	39	4 40	2	58	4 40
3	33	3 55	3	62	4 48
4	36	3 50	4	72	4 40
5	31	4 10	5	64	4 30
6	32	4 05	6	67	4 35

To each 0·25 ml. serum, 0·025 ml. streptokinase solution was added; this mixture was allowed to stand for 30 min. at 37° C. To this mixture 0·25 ml. purified fibrinogen solution was added and 0·025 ml. thrombin (10 units/ml.) was added to produce the clot. The time required for complete lysis at 37° C. was noted in each case.

Heavy fatty meals, particularly when eaten by atherosclerotic patients, will have, as would be expected, an immediate effect on fibrinolysis. An increase in the phospholipid content of the blood under these conditions has been reported[13] and their importance in clotting has been also demonstrated[9]. Under these conditions one might even expect a reduction in clotting time.

It thus appears that the primary cause of death among atherosclerotic patients after a heavy, fatty evening meal is the failure on the part of the circulating blood to cause lysis of small clots formed in small arteries. However, the positive effect of phospholipids on blood clotting must not be overlooked, since this effect is at least partly responsible for enhancing clot formation. The relative frequency of attacks among aged people of coronary thrombosis in the evening or after retiring may possibly be related to the above observations.

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BIOPHYSICS

Effects of Ultrasonic Radiation in *Escherichia coli B* using Fluorochrome Acridine Orange as a Vital Stain

Strugger[1], one of the pioneers who introduced acridine orange as a biological fluorochrome, observed that dead cells take up more of this dye, and under ultra-violet excitation fluoresce red, whereas living cells take up less dye and fluoresce green. This difference in the fluorescence is often used as a test for viability of cells and is referred to as 'Strugger effect'[2]. Loss of viability associated with red fluorescence has also been confirmed by Krebs and Gierlach[3] in their work involving radiobiological action on *Allium cepa* cells. Later work has shown that green acridine orange fluorescence in normal cells is to be associated with cell constituents rich in deoxyribonucleic acid[4]. It is also known from the observations of Beers *et al.*[5], Bradley and Wolf[6], and Ranadive and Korgaonkar[7], that deoxyribonucleic acid can form two complexes with acridine orange. One of these complexes is formed when the relative concentration of acridine orange to deoxyribonucleic acid is low, and exhibits strong green fluorescence and the other occurs when this ratio is high and shows orange or red fluorescence. Shift of fluorescence from green to orange is a critical step in this transition, whereas further change from orange to deep red is not sharp and occurs with further increase in concentration of acridine orange, without involving formation of new complexes. 'Strugger effect' may be explained in terms of these observations as a kind of damage to structures rich in deoxyribonucleic acid in the inactivated cells. This results in their high uptake of acridine orange to such an extent that the corresponding fluorescence is copper red. Few observations, however, are available to indicate the nature and extent of damage near the critical point when the shift of fluorescence from green to orange just occurs. A study of this nature in relation to viability was carried out by us on *E. coli* using ultrasonic waves for irradiation and the findings are reported here.

The ultrasonic generator used in this work consisted of a radio-frequency oscillator and a high-voltage power supply unit built in this laboratory by one of us (V. G. T.). The output of the oscillator was link-coupled to a barium titanate transducer having a resonant frequency 1·6 Mc./sec. The transducer was in the form of a tube 2 in. long and 1 in. inside diameter, into which the glass tubes containing bacterial suspensions were introduced. The transducer was kept immersed in transformer oil which acted as a coupling medium for ultrasonic energy from the transducer to the experimental material. The transducer was worked at its resonant frequency, which was continuously checked during the observations with a loosely coupled wave meter (General Radio type 556*A*). The power of the ultrasonic generator was controlled by using a 'Variac' in the primary circuit, and the monitoring was carried out continuously during irradiation with the help of a 2·5-amp. resonant frequency meter in series with the transducer and a vacuum tube voltmeter across it. A Rhode and Schwartz electronic multimeter type *URI BN* 1050 was used for the purpose. During all the exposures the current passing through the transducer was kept constant at 1 amp. and the voltage across it 10·9 V. under loaded conditions. The resonant frequency power fed to the transducer under these conditions worked out to be ≈ 0·25 watt/cm.^{3}. Even for the highest exposure employed the overall heating of the suspensions was within 2 deg. C.

Escherichia coli strain *B* obtained from the National Chemical Laboratory of India, Poona, was used. Inocula from fully grown agar slants were allowed to grow in nutrient broth (Difco), for 24 hr. at 37° C.

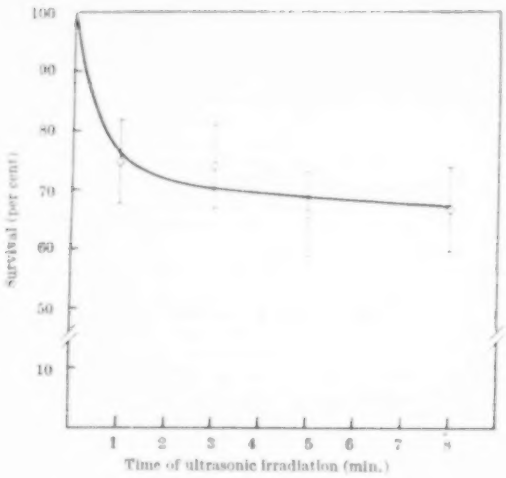

Fig. 1

The organisms were centrifuged, the pellet washed twice and finally suspended in 4·5 ml. buffered saline (*p*H 7·4). Aliquots of 0·5 ml. from such suspensions were diluted (1 : 10) and exposed to different doses of ultrasonic radiation maintaining suitable controls. The cells were assayed for viability by adopting the standard plating technique. Sterile conditions were maintained throughout the work and observations were repeated several times. The results of a typical set are shown in Fig. 1.

For the examination of fluorescence, measured quantities of control and treated bacterial suspensions were mixed with equal volumes of acridine orange solutions (conc. 0·05 per cent) in veronal buffer (*p*H 5·3). After an interval of 10 min., smear preparations of the stained material were made on glass slides (Gold-seal). The fluorescence of the vitally stained material was observed under a Reichert 'Lux U.V.' fluorescence microscope. A mercury arc lamp with a blue transmitting filter No. 8027 was used as a light source and blue cut-off filter No. 8006 was placed over the eyepiece.

In the untreated population, green fluorescence was observed, in almost all the cells. Preparations receiving even a few seconds exposure to ultrasonic radiation showed cells with orange fluorescence. Exact cell count was not possible under the limited magnification available with the fluorescence microscope. The occurrence of orange fluorescing cells increased with the dose, and with about 1 min. exposure almost the entire population turned orange. Further treatment did not show any noticeable change in this fluorescence within the dose-range covered in these experiments.

Some of the ultrasonically treated suspensions were inoculated into liquid media, allowed to grow, and observations on fluorescence were made as above on these. Orange fluorescence was noted, and cells with green fluorescence could scarcely be observed. Confirmatory evidence for the persistence of orange fluorescence in the subsequent generations was obtained from the observations on cells picked up from isolated colonies grown on nutrient agar plates, from the treated suspensions.

The salient points from these observations are: (1) Ultrasonic treatment at the intensity-level employed shows about 25 per cent loss in viability in *E. coli* after 1 min. of exposure and no appreciable further loss is noted even with prolonged treatment up to 8 min. (2) Such a treatment also causes a shift of fluorescence from green to orange on staining the cells with acridine orange. (3) An exposure of 1 min. is sufficient to bring about such a change in fluorescence in almost the entire population. There is no indication of a threshold dose even at the lowest dose employed. (4) The altered response to acridine orange staining persists in the subsequent generations observed.

From these findings it appears that if copper red fluorescence is to be associated with total inactivation of the cells as observed by Strugger and other workers, there is a wide gap in the cell damage between such a stage and the point close to the critical shift of green fluorescence to orange. More than 70 per cent of the cells showing orange fluorescence are found to retain their viability. Thus, the capacity for growth of the cell as a whole as well as the replication potential of its genetic material (which is considered to be chiefly involved in the fluorescence shift) is retained to a large extent. The cell at this stage seems to be physiologically closer to the normal cells than to the totally inactivated ones. Besides, there is an indication that it has acquired a degree of resistance to ultrasonic inactivation. The observed persistence of the altered response to acridine orange staining on sub-culturing is also interesting from its genetic implications and needs further investigation.

One of us (S. S. R.) expresses his thanks to the Council of Scientific and Industrial Research (India) for the award of a research fellowship, during the tenure of which this work was carried out.

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RADIOBIOLOGY

Retention of Zinc-65 in the Bones of Rats

The distribution and retention of zinc-65 in the organs and tissues of both normal and tumour-bearing animals has been studied extensively[1-4]. Most of these observations, however, have extended only over short periods following administration of zinc-65 and little attention has been paid to the retention of the isotope in bone. Ballou[5] and Gilbert and Taylor[6], in work extending over periods of up to 300 days, have shown that there is a prolonged retention of zinc-65 in bone.

In the present investigation the retention of zinc-65 in the bones of rats has been observed over

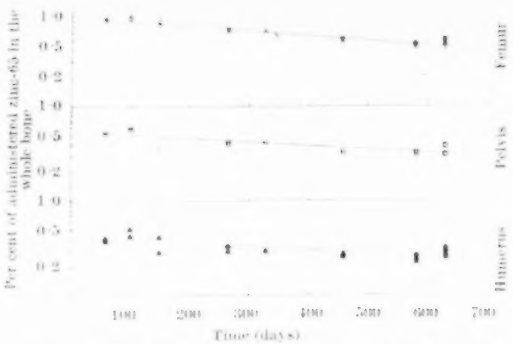

Fig. 1. Retention of zinc-65 in the femur, pelvis and humerus of 'August' rats

a period of 630 days following intravenous injection of the isotope.

The animals used were male rats, seven weeks old, and of the highly inbred, brown-hooded, August strain. Each animal received 2 μc. zinc-65 administered intravenously as a 'zinc-65 serum protein complex'. The preparation of this complex and other experimental details have already been described[4]. The animals were killed in pairs at varying times after injection and the femur, humerus, pelvis and ribs were assayed for zinc-65 and total zinc content.

The retention of zinc-65 in the femur, pelvis and humerus over the period from 58 to 630 days after injection is shown in Fig. 1. In each case it will be seen that, over this period, the retention can be described by a single exponential function. The equation for each bone, together with the appropriate half-times and the standard error of the rate constants, are given in Table 1.

Table 1

Bone	Equation	Half-time (days)	Regression coefficient S.E.
Femur	$0{\cdot}91\,e^{-0{\cdot}00116t}$	598	$0{\cdot}00116 \pm 0{\cdot}00012$
Pelvis	$0{\cdot}56\,e^{-0{\cdot}00092t}$	752	$0{\cdot}00092 \pm 0{\cdot}00015$
Humerus	$0{\cdot}40\,e^{-0{\cdot}00074t}$	941	$0{\cdot}00074 \pm 0{\cdot}00017$
Mean	—	738	$0{\cdot}00094 \pm 0{\cdot}00024$

The specific activities of zinc-65 in the various bones are shown in Table 2. It will be seen that, 7 days after injection, the zinc-65 has been distributed approximately uniformly throughout the zinc contained in the skeleton. The total zinc content of all the bones which were examined continued to rise throughout the period of observation; the values shown in Table 3 indicate that the zinc content of the femur, pelvis and humerus, expressed as μgm. zinc/gm. of bone, do not differ significantly from each other at any age. The zinc content of the ribs does not increase as much as that of the other bones.

Table 3. Variation of Zinc Content of Bones with Age

Age (days)	Femur	Humerus	Pelvis	Ribs	Mean (excluding ribs)
56	77 ± 7	83 ± 5	70 ± 6	85 ± 6	77 ± 3
103	104 ± 2	99 ± 5	101 ± 6	83 ± 4	102 ± 2
149	102 ± 5	116 ± 6	103 ± 18	71 ± 0	107 ± 6
198	105 ± 3	117 ± 13	102 ± 2	112 ± 7	110 ± 5
313	133 ± 8	130 ± 15	146 ± 3	105 ± 8	136 ± 5
679	191 ± 5	198 ± 11	211 ± 8	149 ± 12	200 ± 4

Zinc content of bone, μgm. zinc/gm. wet bone ± standard error. All values are means of results from 2 animals except values for 679 days. These represent the mean for 4 animals.

The half-times for the retention of zinc-65 in the three bones are probably not significantly different from each other, although it appears that retention in the humerus is more prolonged than in the other two bones. The half-time reported here for retention in the femur is somewhat greater than the value which may be inferred from the results reported by Ballou for the retention of zinc-65 in the femur of Sprague-Dawley rats.

The mean half-time for the retention of zinc-65 reported here is much shorter than the corresponding half-time of 1,610 days for the retention of calcium-45 in the bones of rats of the same age and strain (Taylor, D. M., unpublished observations).

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Assessment of Dietary Strontium-90 through Urine Assay

Since the manner in which the body handles ingested strontium is quite well established[1–3], the chief problem of determining the relative strontium-90 hazard from food concentration data is that of defining the overall average diet with precision. Thus the usual problems concomitant with obtaining dietary intake for nutritional or other purposes apply. In addition to this there is the rather severe problem, generally of minor importance with respect to nutrients, of selecting for assay representative aliquots

Table 2. Specific Activity in Percentage of Injected Activity/mgm. Zinc

Time (days)	7		58		100		149		264		630			
Animal No.	1	2	3	4	5	6	7	8	9	10	18	19	20	21
Femur	42 39	37 30	13·1 12·7	12·2 11·2	11·4 11·4	11·8 11·8	7·4 —	9·1 9·1	4·9 4·8	5·6 6·2	2·3 2·5	1·9 1·8	2·4 2·3	2·3 2·3
Humerus	31 33	32 34	11·3 13·2	11·3 10·9	13·9 13·7	9·5	6·5 6·5	9·2 11·3	6·1 6·2	5·7 5·6	3·1 2·3	3·5 3·1	3·0 2·6	2·7 —
Pelvis	40	34	12·1	11·5	13·5	10·0	7·1	10·3	3·7	5·0	2·1 2·1	1·7 1·6	1·6 —	1·8 2·0
Ribs	27	27	15·1	10·0	11·9	13·5	8·3	6·1	4·0	4·9	0·7	1·1	0·5	1·1

of individual food items. Whereas differences in the vitamins or mineral content by a factor of two are rare for a given food, differences in strontium-90 content by a factor of ten or more are not uncommon[4].

The variations due to latitude[5] and rainfall[6] have long been recognized. In addition, the pattern of rainfall during the growing season is also critical, particularly with respect to cereals[7]. Thus wheat grown on fields only a few miles apart may differ markedly if one got a local shower two weeks before harvest and the other did not.

In view of these problems, it was proposed to use urinary concentration as an independent index of strontium-90 ingestion. By virtue of interchange with soft tissues and other labile strontium-90 depots, such a sample would represent some averaging of the ingestions over a period of days, although the most recent meal would play the most dominant part. Such a sample would also circumvent the problem of getting diet information which may be biased due to the presence of the observer. One can bring additional food to a few meals or think of extra items for an interrogator with much more facility than he can change his excretion-rate.

A study of dietary strontium-90 in particular military groups, together with its concentration in corresponding urine, has been conducted in three countries in co-operation with the Interdepartmental Committee on Nutrition for National Defense of the National Institutes of Health and Department of Defense. The Committee regularly conducts dietary surveys in connexion with nutrition studies in various countries around the world. Representative composite diets are obtained for nutrient assay and aliquots of these have also been used to determine dietary strontium-90. In a number of the local investigations of military units large samples (approximately 12–15 litres) of urine were also obtained, these being random collections representing a large number of men in each case.

Comparative data on diet and corresponding urine for various locations in Peru, Ecuador and Vietnam are given in Table 1. It is noted that the food/urine concentration ratio in terms of μμc. strontium-90/gm. calcium is approximately 2 on the average in each of the three countries investigated. The relation is about the same on the rice diet of Vietnam, which is relatively high in strontium-90 as in Peru and Ecuador. It is concluded from these results that for monitoring purposes strontium-90 concentration in urine gives a reasonable index of the dietary level.

Table 1. Comparison of Strontium-90 Concentration in Food and Urine, *μμc.* Strontium-90/gm. Calcium

	Food	Urine	Ratio
Peru			
Arequipa	2·72	1·31	2·1
Lima	2·49	1·72	1·4
Piura	1·76	0·93	1·9
Pumbes	2·53	1·21	2·1
			Ave. 1·9 ± 0·2
Ecuador			
Cuenca	1·02	0·67	1·5
Guayaquil	1·54	0·54	2·9
Loja	2·95	1·41	2·8
Machala	3·71	1·50	2·5
Quito	0·84	0·45	1·9
Salinas	3·00	1·35	2·2
			Ave. 2·3 ± 0·4
Vietnam			
Bien Hoa	3·5	4·0	0·9
Quang Trung	6·9	3·7	1·9
Duc My	14·8	3·9	3·5
Danang	17·0	8·5	2·0
			Ave. 2·1 ± 0·7

The question of which of the two indices is the more reliable under these conditions of field operations cannot be answered on the basis of the present findings; but there is an indication that the urine values may be the better of the two. Whereas the mean deviation of the individual ratios from the average is 12 and 18 per cent in Peru and Ecuador, it is 33 per cent in the case of Vietnam. This may reflect two special difficulties encountered with the Vietnam diet. In Vietnam the diet is composed of more than 80 per cent rice and, as noted, grains in particular fluctuate markedly in their strontium-90 content. Thus an individual food composite taken on a given day would be less representative of the overall picture than the same sample taken in Western culture or South America. Secondly, small fish, shrimp, etc., which commonly make up a portion of the Vietnam diet, are typically incorporated into the 'stew' and may be eaten, bones and all. Strontium-90/calcium ratio in fish is generally very low compared with other foods, and thus this fluctuating parameter would also reduce the validity of short-term composite diet data with respect to the strontium-90 component.

It is concluded that: (1) composite food and urine data on the population groups reveal that the food/urine concentration ratio of strontium-90 in terms of μμc. strontium/gm. calcium is about two; (2) for monitoring purposes, the urine strontium-90 concentration is a satisfactory index of ingestion. Urine data may be the more reliable under some conditions of field observation.

This work was supported by the U.S. Atomic Energy Commission under contract *AT* (30–1)–1656. The food and urine samples were collected by survey teams of the Interdepartmental Committee on Nutrition for National Defense. Team members of particular note in this phase of the survey included Jerome Uram and Ogden Johnson (Peru), Gerald Combs and Alvin Wolfe (Ecuador) and C. Frank Consolazio and Albert N. Booth (Vietnam).

The strontium-90 analyses were conducted by Rieta Slakter Hirshman and Karin Bartelsen of the Lamont staff.

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HISTOCHEMISTRY

Detection by Fluorescence of Oxytetracycline bound to Bone

Milch, Rall and Tobie[1,2] observed the property of antibiotics of the tetracycline series of becoming localized specifically in bony tissue formed during the administration of these drugs, and persisting in the zone of localization until the structural remodelling has caused the absorption of the bony areas which

have bound the tetracyclines. This observation seemed likely to offer a practical and useful method of vital staining, especially for the detection of the turnover of bone.

In fact, the tetracyclines, which are fluorescent in ultra-violet light[3], preserve this property even when bound to bony tissue, and therefore it is possible to detect them by fluorescence microscopy[1,2]. Obviously, if the time pattern of the administration of the drugs is known, it is possible to determine directly the age of the fluorescent bony structures and indirectly the value of the bone-forming activity and its topographical distribution.

As the tetracycline bound to bone is dissolved with bone salts, histological methods which imply decalcification must be avoided. Consequently, the observations of Milch *et al.* were carried out on undecalcified sections prepared by a freezing rotatory microtome; the limited size of sections obtained by this method inevitably is a disadvantage.

I found that fixation in formaldehyde, in alcohol, or in acetone modifies, but does not destroy, the fluorescence of oxytetracycline bound to bone. Thus I was able to use the method of Sognnaes *et al.*[4], embedding the specimens in methyl methacrylate and preparing sections ground with emery paper. In this way the sections obtained are thin enough for the perfect detectability of fluorescence in the microscope.

All this is strictly necessary when the specimens to be examined consist not only of bone but also of soft tissues. The details of this method, which permits the study of sections of unlimited size, together with the technique used in fluorescence microscopy, have been described elsewhere[5].

The results obtained with experimental material and from biopsy and necropsy specimens reveal that the method of vital staining of bone with tetracyclines has a significant advantage over the common method of labelling bone with isotopes. In fact, the optical resolution in fluorescence microscopy is much higher than that allowed by the granular form of autoradiographic emulsions.

In sections prepared by embedding in methyl methacrylate and grinding, the fluorescence is distributed in different patterns according to the structure of the bony tissue. In actively growing bones mainly of a parallel-fibred, finely bundled structure, one can observe yellow fluorescent areas alternating with other areas without yellow fluorescence.

In adult animal and human bone, which mainly consists of lamellar bone, one can observe at times large and homogeneously yellow fluorescent rings or bands, composed of various 'lamellae', and at other times, thin yellow fluorescent rings or lines, arranged singly or serially, composed of only one 'lamella'.

As a rule, different values of mineralization correspond microradiographically to the differences in age as revealed by the fluorescent areas (see Fig. 1).

In adult human lamellar bone, the persistence of tetracycline fluorescence localized in bony tissue has been observed more than seven months after administration, with some variations in intensity and colour of the emitted fluorescent light. This persistence is determined by the quickness of the remodelling process and, perhaps, by differences in mineralization patterns of bony tissue.

These results will be discussed more fully elsewhere.

This method, with its specificity and its advantages as compared with the radioisotope-labelling method, can be appropriately applied to the study of any physiological and pathological bone problems which require a precise knowledge of the age of the structures. It would indeed be very useful to have a complete understanding of the chemical nature of the binding of tetracyclines to bone, as this would allow a better explanation of the mineralization of the bone.

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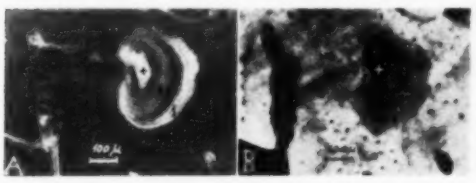

Fig. 1. Undecalcified section, 50μ thick, from the radius of a three-year-old dog, which received three successive administrations of oxytetracycline. (*A*) shows the fluorescence in white; (*B*) is the microradiograph of the same field. The first administration of oxytetracycline is represented in (*A*) by three fluorescent parallel rings (1), the second by two fluorescent rings (2), the third by the fluorescence of the central osteoid edge of the Haversian system (+)

Histochemistry of Human Sublingual Glands

BIOLOGICAL work on salivary glands has revealed that sialic acid is the only acidic component in the bovine submaxillary gland and probably in the sublingual gland of the rat[1-3]. These findings resulted in the elaboration of a method for the removal of sialic acid in tissue sections known to contain abundant amounts of this sialo-mucin[4,5]. Such a method consisted of exposing the sections to acid hydrolysis at different *p*H's and temperatures.

It was then decided to evaluate human sublingual glands histochemically using alcian blue, safranin *O*, and azure *A* for acidic polysaccharides and periodic acid–Schiff for glycoproteins. The glandular mucous acini always showed metachromasia with azure *A* and safranin *O* and a great affinity for alcian blue and periodic acid–Schiff.

Sections of tissue were then incubated in Walpole buffer solutions at *p*H 2·5 at 55° C. and 80° C. for 2–16 hr. It was found that only incubations at 80° C. for 16 hr. resulted in a slight loss of alcian blue and azure *A* staining, and considerable diminution in safranin *O*-positive material.

In an attempt to classify the nature of the substance or substances that presumably were not affected by mild acid hydrolysis, sections were exposed to the action of testicular hyaluronidase for varying periods of time of 1–3 hr. This procedure did not reverse metachromasia or the affinity for alcian blue, thus indicating that the acinar material contained sul-

phated polysaccharides other than chondroitin sulphate *A* and/or *C*, which are readily hydrolysed by hyaluronidase. In order to determine whether chondroitin sulphate *B* or a closely related substance was present in the acini, tissue sections were then incubated in 1 *N* hydrochloric acid at 80° C. for 10, 30 and 60 min. This treatment caused only a partial decrease in staining.

Because chondroitin sulphate *B* may be removed by acid hydrolysis, these findings would seem to suggest that human sublingual glands contain a heparin-like substance alone or in addition to a sialo-mucin.

Incubations of tissue sections in papain and pepsin for periods of time up to 1 hr. did not affect the periodic acid–Schiff, alcian blue and metachromasia, while prolonged incubations (3 hr.) diminished the staining reactivity of the acini. These findings are opposite to those observed in bovine submaxillary and rat sublingual glands, in which even short incubations with either proteolytic enzyme completely removed all the staining materials. The observations relative to human sublingual glands would indicate that significant species differences exist in the composition of salivary mucins. These results are also of interest in the light of the results reported by Pusztai and Morgan[6] on their work on the effects of papain and ficin on blood-group-specific mucopolysaccharides. These authors demonstrated that dialysis following exposure to proteolytic enzymes failed to reveal demonstrable amounts of sugars and oligosaccharides.

These findings, together with the observation by Tasiro[7] that human sublingual gland is one of the richest sources of blood-group substances, suggest the possibility that some of the polysaccharides in human sublingual mucin are closely related to blood-group substances.

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PATHOLOGY

Induction of Melanotic Tumours in the White ('Partial Albino') Syrian Hamster

Della Porta *et al.*[1] first reported the induction of melanotic tumours in the skin of Syrian golden (agouti) hamsters after topical applications of 7,12-dimethylbenz(*a*)anthracene (DMBA). This finding was afterwards confirmed by these and other investigators[2–4]. Ghadially and Barker[5] have postulated that the melanotic lesions arise from dermally situated perifollicular networks of melanocytes intimately associated with certain hair follicles. They suggest that the proximity of dermal melanocytes to sebaceous glands of hair follicles renders them especially vulnerable to the action of carcinogens topically applied to the skin. Recently, Illman and Ghadially[6] have reported the induction of melanotic tumours in the general body skin of white ('partial albino') Syrian hamsters during repeated topical applications (22 weekly treatments) of 2 per cent DMBA in acetone. It is noteworthy that white hamsters characteristically possess a white hair coat, and grossly detectable pigmentation is restricted to the skin of the ears, perineum and genitals; a darkening of eye colour may occur with advancing age[7,8]. Whiteness of hair coat is a genetically determined trait inherited as a simple Mendelian recessive[7,8]. The purpose of this communication is to report observations made in our laboratory on the occurrence of melanotic lesions in white hamsters treated with DMBA.

In our experiments, initiated without knowledge of those of Illman and Ghadially[6], 10 male and 10 female random-bred white hamsters, 4 months old at the start, were treated once weekly for 3 consecutive weeks with a 1 per cent solution of DMBA (Eastman) in mineral oil, essentially the same procedure as that of Shubik *et al.*[2]. Before the first treatment, the hair was shaved from the backs of all animals by means of electric clippers. Each treatment consisted of the delivery by pipette of 4 evenly spaced drops of the carcinogenic solution to this region. It was estimated that each drop of solution represented a delivered volume of 20–30 µl.; that is, it contained 200–300 µgm. DMBA.

Raised nodules were observed in the treated areas 15 weeks from the start[2]. Undoubtedly, they were present prior to this time, for some lesions were already 3–5 mm. in greatest diameter. The vast majority did not exceed a diameter of 2 mm. and in many cases appeared flat to gross inspection. By the eighteenth week, more nodules were evident, and many of the older ones had increased in size. The nodules ranged in colour from pink-white through brown to an intense black. Certain lesions recorded as pink on first observation were noted as grey-black 3 weeks later. Both light and dark nodules were present in the same animal, and there was no clear correlation between nodule size and gross pigmentation. Of 20 hamsters, 19 survived to the fifteenth week after treatment. Of these, 18 had at least one nodule at that time. The remaining hamster, a male, showed evidence of raised nodules by the eighteenth week after treatment.

Shubik *et al.*[2] have designated pigmented nodules exceeding 2 mm. as melanotic tumours. At the time of writing (20 weeks), 8 surviving females have a total of 34 spots 2 mm. or more in greatest diameter on the dorsum, including the tail; the corresponding value for 8 surviving males is 44. Although occasional lesions now exceed 6 mm. in diameter, most lesions are as yet smaller than 2 mm. The total population of dorsal spots on surviving hamsters is now 99 for the females and 112 for the males. In addition, 11 pigmented lesions have been noted in or near the margins of the eyelids. These lesions vary from deep red to black in colour, and one is now approximately 7 mm. in diameter. Such lesions have not been reported previously for the white or pigmented hamster. It is possible that the spread of the carcinogen through wiping would account for the occurrence

of pigmented lesions outside the areas directly treated with DMBA. No association of the costovertebral spots with pigmented lesions has as yet been noted.

Microscopically, the dorsal lesions appear quite similar to those described by Illman and Ghadially[6] for the white hamster, and by Della Porta *et al.*[1] and Ghadially and Barker[5] for the golden (agouti) hamster. A variable content of melanin granules would appear to be directly correlated with gross observations of the colour of the lesions. As previously reported[5], the pigment granules react positively with silver staining (Fontana) and are bleached by potassium permanganate. The lesions are highly vascularized, and are composed of cells mainly polyhedral or spindle-shaped. They are clearly dermal in location, although they intimately invest hair follicles[5,6]. The association of the melanotic tumours with hair follicles is especially evident in serial sections of skin where care is taken to obtain longitudinal sections of hair follicles. In some instances, the impression is gained that the lesions merge with follicular structures. The proximity of melanotic lesions to hair follicles provides further evidence that the pilosebaceous apparatus is an important channel for the entry of topically applied carcinogens into skin[6,9].

Nevertheless, the origin of melanotic lesions in the white hamster is as yet uncertain, for perifollicular networks of melanocytes have not been identified in this variety by Illman and Ghadially[6] or by us. It has been suggested[6] that melanotic tumours in white hamsters are derived from a system of amelanotic perifollicular melanocytes. Indirect evidence supporting this view is our preliminary observation that repeated topical applications of croton oil result in an increased number of perifollicular melanocyte nests in the golden hamster. Thus it would appear that dermal melanocytes may be present in an amelanotic state, at least in this variety of hamster. The possibility that melanotic lesions are derived from hair follicles cannot as yet be entirely excluded. This explanation has been given by Szabó[10] for the origin of melanotic spots in pigmented mice treated with DMBA and croton oil. It is hoped that the present experiments dealing with the effect of repeated topical applications of croton oil on white hamsters will shed some light on this problem.

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Toxicity and Anti-leukæmic Effectiveness, in Mice, of 4-Amino-4-deoxy-N^{10}-methyl-5,6,7,8-tetrahydropteroylglutamic Acid (Tetrahydroamethopterin)

It has recently been reported[1] that the 5,6,7,8-tetrahydro derivatives of the folic acid antagonists aminopterin, N^{10}-formylaminopterin and amethopterin have a greater inhibitory action on the growth of *Streptococcus faecalis R* and *Pediococcus cerevisiae* than the unreduced analogues. It was therefore of interest to determine whether the greater inhibitory action found in the bacterial system is also reflected in a mammalian system, by an increase in host toxicity and/or anti-leukæmic activity.

Amethopterin and its tetrahydro derivative were chosen for a comparative study. The former is used regularly in our Laboratory[2] as a standard drug for the evaluation of new anti-leukæmic agents, and its toxicity to normal mice is well established. Tetrahydroamethopterin was prepared according to the method of Kisliuk[1,2], and for injection was dissolved in a vehicle of 0·6 per cent potassium ascorbate in 2 per cent aqueous sodium bicarbonate. The solution was stored frozen in rubber-sealed vials under hydrogen in the dark. Under these conditions, tetrahydroamethopterin appears to be stable for several days. Amethopterin was also dissolved in the ascorbate-bicarbonate mixture.

Hybrid male *CIBA* mice [(*BALB cAn* × *DBA* 2*J*)F_1], 12–13 wk. old and weighing 24–28 gm. at the beginning of the experiment, were used in this work. Normal mice, mice bearing advanced leukæmia *L1210* (amethopterin-sensitive) and mice bearing advanced leukæmia *L1210–M46R* (amethopterin-resistant)[4] were divided into groups and given daily subcutaneous injections of the drugs at 0·01 ml./gm. body-weight. Vehicle and untreated controls were included in each experiment. Records were kept of the weights of the animals and, in the tumour-bearing animals, of the local tumour size.

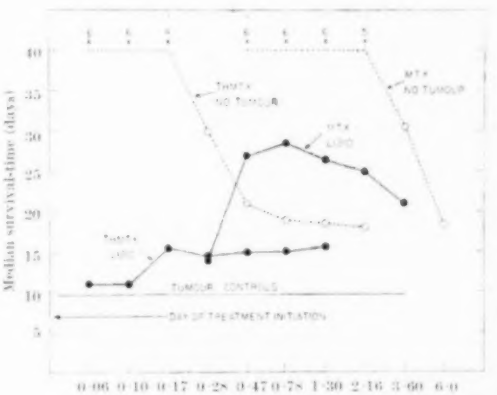

Fig. 1. Toxicity and anti-leukæmic effect of amethopterin (MTX) and tetrahydroamethopterin (THMTX). ○, normal mice, 6 per group; ●, tumour mice, 10 per group. The tumour mice were inoculated subcutaneously in the right inguinal region with about 2×10^5 cells of leukæmia *L1210* on day 0. Daily treatment was initiated on day 7 after inoculation and continued until the end of the experiment. Treatment of the normal mice was begun on the same day as that of the leukæmic mice. The numerals above the vertical arrows refer to the number of mice in each group which survived until day 40, at which time the experiment was terminated

Table 1. Effect of Citrovorum Factor (CF) on the Toxicity of Amethopterin (MTX) and Tetrahydroamethopterin (THMTX) in Normal Mice

Drug	Drug administered alone			Drug administered concomitantly with 20 mgm./kgm./day CF		
	Dose (mgm./kgm.)	Survivors* day 14	Median survival time (days)	Dose (mgm./kgm.)	Survivors* day 14	Median survival time (days)
MTX	40	0	5	160	0	9·5
	20	0	5	80	4†	> 14
	10	0	8	40	6	> 14
	5	1†	12	20	6	> 14
	2·5	6	> 14	10	6	> 14
	1·25	6	> 14	5	6	> 14
				2·5	6	> 14
THMTX	10	0	11·5	80	0	9·5
	5	0	9·0	40	5†	> 14
	2·5	0	10·0	20	6†	> 14
	1·25	0	10·5	10	6	> 14
	0·625	1†	13·5	5	6	> 14
	0·31	6†	> 14	2·5	6	> 14
	0·16	6	> 14	1·25	6	> 14
				0·625	6	> 14
				0·31	6	> 14

* Six mice per group; each group received daily treatment from day 0 to day 13.
† Mice receiving these dosage-levels had lost considerable body weight by day 14. Other studies of the toxicity of MTX and THMTX in normal mice (Fig. 1) suggests that these animals would have succumbed to continued treatment.

Fig. 1 shows the results obtained for normal mice and mice bearing advanced leukæmia *L*1210. The results obtained with advanced leukæmia *L*1210–*M*46*R* are not included as neither drug caused an increase in survival time over the untreated or vehicle controls, at any of the doses indicated. This would seem to indicate a complete cross-resistance for the tumour to the tetrahydroamethopterin. The toxicity of tetrahydroamethopterin on a daily treatment schedule, in normal mice, was about ten times that of amethopterin. The toxicity of both drugs was manifested by a 25–30 per cent body weight loss prior to death, and the marked melæna observed would indicate severe gastrointestinal mucosa damage (more marked in the case of tetrahydroamethopterin).

With advanced leukæmia *L*1210, amethopterin gave a typical bell-shaped curve when survival time was plotted against logarithm of dose[4]. In contrast, tetrahydroamethopterin gave a flat curve over a similar dose range (0·17–1·30 mgm./kgm./day), and the survival-times in this region were considerably less than for the optimal dose of amethopterin (0·78 mgm./kgm./day). In a second experiment with the tetrahydro derivative a similar flat curve was obtained, and the median survival-time of the mice did not decrease until a dose of 52 mgm./kgm./day was used.

Although both drugs brought about a reduction of the local tumour size during the course of treatment, an effective dose of tetrahydroamethopterin, for example, 0·17 mgm./kgm./day, was attended by considerable loss of weight of the host. This is in contrast to amethopterin, where an effective dose, for example 0·78 mgm./kgm./day, caused no loss of weight over the same time span. Thus, it appears that toxicity to the host is a severely limiting factor in the treatment of advanced leukæmia *L*1210 with tetrahydroamethopterin.

Since previous work has shown[5] that the toxicity of folic acid antagonists, in mice, can be nullified by the concomitant administration of citrovorum factor, but not by injecting folic acid at the same time, it was of interest to determine whether the same relationships existed between tetrahydroamethopterin and these metabolites. To this end, a series of normal *CDBA* mice was given daily doses of amethopterin or tetrahydroamethopterin ranging from non-toxic to toxic levels. A parallel series received 20 mgm./kgm./day of citrovorum factor (calcium leucovorin) with the drug. The results are shown in Table 1. Citrovorum factor gave complete protection from frankly toxic doses of both drugs. However, in a second experiment in which 20 mgm./kgm./day of folic acid was administered concomitantly over the same dose ranges of the drugs, no protection from toxic doses of either drug was observed. The above observations suggest that amethopterin and tetrahydroamethopterin are acting by similar mechanisms in so far as their toxicity to normal mice is concerned.

It is also of interest to note that the diminished antileukæmic effectiveness of tetrahydroamethopterin, relative to amethopterin, is paralleled by a diminished ability of the drug to inhibit purine biosynthesis

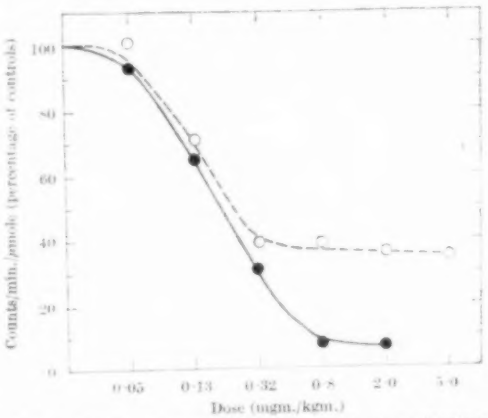

Fig. 2. Effect of amethopterin (●) and tetrahydroamethopterin (○) upon the incorporation *in vivo* of carbon-14 labelled formate into the acid-soluble adenine of mouse spleen infiltrated with leukæmia *L*1210. The experiment was carried out on day 8 after leukæmic inoculation. The mice were given a subcutaneous injection of the drug, then 20 min. later an intraperitoneal injection of 200 μc./kgm. of carbon-14 labelled sodium formate, and were killed after another 20 min. Acid-soluble adenine was isolated from the pooled spleens of three mice, and its specific activity determined (ref. 6). Untreated controls received 2 per cent sodium bicarbonate solution. Results are expressed as

$$100 \times \frac{\text{counts/min./}\mu\text{mole (treated)}}{\text{counts/min./}\mu\text{mole (controls)}}$$

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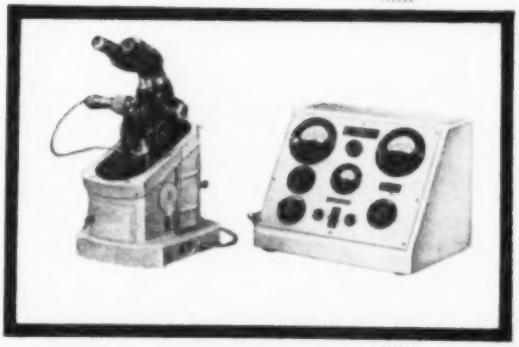

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de novo. Previous investigations in our Laboratory have shown[6] that the inhibition of carbon-14 labelled formate incorporation *in vivo* into the acid-soluble adenine of leukæmia-infiltrated mouse spleen can be related quantitatively to the dose of amethopterin administered to the animals. Fig. 2 shows the dose-response curves obtained with amethopterin and tetrahydroamethopterin in this system. It can be seen that, at low doses, both drugs produced similar partial inhibition. However, beyond a level of about 0·32 mgm./kgm. of tetrahydroamethopterin, no increased inhibition was observed. This is in contrast to the marked inhibition produced by higher doses of amethopterin.

The present work has shown that tetrahydroamethopterin is more toxic to normal mice than is amethopterin at equivalent dose-levels. In mice bearing advanced leukæmia *L*1210, tetrahydroamethopterin also appeared to cause somewhat more extensive regression of the local tumour than amethopterin. However, the increased toxicity of tetrahydroamethopterin was proportionately greater than the anti-tumour effect, so that there was a net loss of anti-leukæmic effectiveness. Thus, the toxicity of tetrahydroamethopterin relative to amethopterin for host and tumour cells is, in fact, similar to that reported in the bacterial studies[1]. The biochemical basis for this greater toxicity of tetrahydroamethopterin is not known. One possibility is that it is a more effective antagonist of the reduced, coenzymically active forms of folic acid than amethopterin.

We are doing work on the biological and biochemical activity of the reduced folic acid antagonists.

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Ovine Fœtal Resorption caused by *Toxoplasma gondii* Infection

Wastage in ovine reproduction due to infection of the pregnant ewe by *Toxoplasma* has been described in New Zealand[1,2], Australia[3,4] and the United Kingdom[5]. Experimental infection has on several occasions[1,6] confirmed its role as a cause of perinatal mortality. Following experimental infection, ovine toxoplasmosis has now been observed to cause resorption of the fœtus in addition to perinatal mortality.

Experimental infection of ewes, which were 101–122 days pregnant, was effected by intraperitoneal inoculation with undiluted peritoneal exudate from infected mice. Nine ewes were thus infected and kept under surveillance in a small enclosed pen until parturition. Following inoculation, three ewes showed evidence of a sanguineous discharge at the vulva and were therefore killed.

In one ewe, autopsied sixteen days after inoculation, twin fœtuses, which were partially resorbed, were still distinguishable and the placentomes remained intact, although the intercotyledonary component of the fœtal membranes had disappeared. The placentomes showed lesions of focal necrosis similar to those typically seen in cotyledons from infected fœtal membranes[2].

The two other ewes were not autopsied until 30 and 40 days after inoculation, at which stage no fœtus or fœtal membranes remained obvious; however, there was considerable enlargement of the caruncles, these being concave and approximately 1 in. in diameter; a quantity of sanguineopurulent material was also present within the uterus. In view of the fact that the ewes had been under constant observation since inoculation, these findings were taken as presumptive evidence of resorption.

There is no published information concerning total prenatal mortality-rates in flocks in which toxoplasmosis is known to occur naturally; however, results from a Dorset Horn flock in south-eastern Queensland in which perinatal mortality due to toxoplasmosis has been diagnosed, indicate a large discrepancy between the number of ewes apparently conceiving and those eventually lambing. This discrepancy is only partly accounted for by abortions. It is suggested, therefore, that in some circumstances, fœtal resorption may be more important than perinatal mortality as a manifestation of ovine toxoplasmosis.

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BIOLOGY

Genetic Control of Oxytetracycline Biosynthesis

More than ten years ago Bonner[1] made an unsuccessful attempt to use inactive variants and biochemical mutants of *Penicillium chrysogenum* for studying the mechanism of penicillin biosynthesis. Since that time the mechanism of the biosynthesis of the antibiotic has apparently not been investigated in this way.

In 1956 we published a paper[2] on the biosynthesis of oxytetracycline by methionine- and niacine-requiring mutants of *Act. rimosus*.

It was shown that both mutants require for the antibiotic production much greater amounts of these substances than is needed for their growth. Repeatedly isolated mutants with methionine and niacin deficiencies had the same properties. These results convinced us of the necessity of investigating the genetical control of the mechanism of the antibiotic biosynthesis, particularly the biosynthesis of oxytetracycline. In this connexion an attempt was made

to obtain balanced inactive mutants of the oxytetracycline-producing organism.

At first, under the action of mutagenic factors, namely, ultra-violet light, X-rays or ethyleneimine, inactive variants were obtained, which practically lost the ability to produce the antibiotic ('zero' variants).

Two groups were observed among a great number of zero variants. One group took the form of colonies with very light to almost cream substrate mycelium and white aerial mycelium ('white' group). The other group formed colonies with dark brown substrate and greyish aerial mycelium, which excreted dark brown to almost black pigment into the culture fluid ('black' group).

When two mutants of the 'white' group were grown together on a liquid complex or synthetic medium, they produced no oxytetracycline, whereas when one mutant of the 'white' group was grown together with a mutant of the 'black' group, the activity markedly increased (Table 1). The plating of the mixed culture in Petri dishes showed that only the starting strains when grown together participated in fermentation. The second examination of the mutants with respect to their activity in a pure culture gave no positive results.

The nature of the antibiotic substance, synthesized on mixed submerged cultivation of two inactive variants of *Act. rimosus*, was studied by means of paper chromatography according to the method described by Selzer and Wright[3]. The antibiotic studied proved to be oxytetracycline.

The results of the determination of the antibiotic produced with the help of both the biological and the colorimetric methods coincide.

The studies on cross-transfers of the mycelium throws some light on the mechanism of interaction between the inactive mutants during the oxytetracycline synthesis. The mycelium of the 'black' mutant *T*572, separated from the culture fluid and washed with sterile water, was transferred into a 48-hr. culture fluid of the 'white' mutants *T*12 and *T*999, separated from the mycelium by centrifugation and filtered through a bacterial filter. In all cases of transferring the mycelium of a 'black' mutant into the culture fluid of a 'white' mutant the biosynthesis of oxytetracycline was observed, while in cases of transferring the mycelium of a 'white' mutant into the culture fluid of a 'black' mutant the synthesis was not observed. The behaviour of the 'black' mutant mycelium transferred into the culture fluid of the active starting strain of *Act. rimosus* was the same (Table 2).

Table 1

Strain	Corn steep liquor medium		Synthetic medium	
	Activity (γ/ml.)	Mycelium weight (mgm. %)	Activity (γ/ml.)	Mycelium weight (mgm. %)
Active starting strain	3,046	1,041	1,900	930
*T*1 (white)	0·55	1,095	0·50	1,042
*T*2 ,,	0·20	435	0·20	285
*T*11 ,,	0·41	1,160	0·55	852
*T*12 ,,	0·90	1,360	0·54	1,020
*T*16 ,,	0·80	1,012	0·70	940
*T*956 ,,	0·29	932	0·22	886
*T*999 ,,	0·50	1,042	0·48	787
*T*572 (black)	20·0	872	0·87	752
*T*1 + *T*572	1,030	1,075	790	890
*T*2 + *T*572	700	1,033	600	898
*T*11 + *T*572	830	1,002	490	897
*T*12 + *T*572	1,000	1,083	780	874
*T*16 + *T*572	600	990	600	854
*T*956 + *T*572	720	1,088	670	798
*T*999 + *T*572	760	930	600	870
*T*2 + *T*956	5·0	860	—	—
*T*2 + *T*999	4·0	956	—	—
*T*12 + *T*956	1·0	924	—	—
*T*12 + *T*999	3·0	926	—	—
*T*16 + *T*956	4·0	656	—	—
*T*16 + *T*999	4·0	905	—	—

Table 2

Combination of the mycelium and the culture fluid	Mycelium weight mgm. %		Activity (γ/ml.)			
	Initial	After 36 hr.	Initial	After 12 hr.	After 36 hr.	After 60 hr.
Culture fluid of *T*12 + mycelium of *T*572	1,290	1,384	0·1	106	480	520
Culture fluid of *T*999 + mycelium of *T*572	1,379	1,468	0·2	130	390	420
Culture fluid of *T*572 + mycelium of *T*12	1,520	1,504	0·8	1·0	0·9	1·0
Culture fluid of *T*572 + mycelium of *T*999	1,580	1,600	0·2	0·4	1·0	0·9
Culture fluid of the active starting strain + mycelium of *T*12	1,424	1,431	230	220	260	210
Culture fluid of the active starting strain + mycelium of *T*572	1,214	1,260	270	400	580	640

On the basis of this fact it is possible to assume that 'white' mutants produce some unknown substance (*x*-substance), which provides the antibiotic synthesis by the mycelium of the 'black' mutant *T*572. It is interesting to note that *x*-substance is present in the culture fluid of the active starting strain of *Act. rimosus*.

The task of further investigations is to elucidate the nature of this substance.

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Modifying Factors of Amino-acid Antagonisms in a Mutant of *Neurospora crassa*

In certain amino-acid-requiring mutants of *Neurospora crassa*, any one of a number of naturally occurring amino-acids can inhibit competitively the utilization of the required amino-acid for growth[1,2]. In the course of determining the inhibition indexes of the inhibitory amino-acids, it was noted that variations in certain experimental conditions would cause significant differences in the observed indexes. The mutant strain *E*-5212 (ref. 3), which responds to either phenylalanine or phenylpyruvate, was used in a study of the various modifying factors. Growth assays were performed in the usual manner using Fries minimal medium[4]. The inhibition index is defined as the ratio of inhibitor to required amino-acid which produces complete inhibition of growth for approximately three days at 27° C.

A mutant strain of *Neurospora crassa* has been described which requires thiamine or thiazole for

Table 1. Effect of *p*H and Temperature on Inhibition Indexes

L-Phenylalanine (μmole)	Inhibition index (L-leucine)	Temperature (° C.)				L-Phenylalanine (μmole)	Inhibition index (L-valine)	*p*H		
		20	25	30	35			5·2	5·6	6·0
0	0	0	0	11	36	0	0	0	0	0
0·5	0	24*	39	65	68	0·1	0	44*	47	46
0·5	10	7	24	38	52	0·1	5	42	46	44
0·5	15	0	0	22	48	0·1	10	40	43	38
0·5	20	0	0	0	43	0·1	20	40	44	0
0·5	40	0	0	0	32	0·1	40	30	0	0
0·5	100	0	0	0	25	0·1	80	0	0	0
0·5	200	0	0	0	22					

* Figures indicate mgm. dry weight.

optimal growth at temperatures below 30° C. but which grows on minimal medium like the wild-type strain at 35–39° C.[5]. This mutant is inhibited by threonine, and the inhibition is most strongly expressed at 35° C. and at *p*H values below 5·8 (ref. 6). Table 1 shows that changes in *p*H and temperature had a much different effect on the amino-acid inhibitions described here than on the threonine inhibition previously reported[3,6]. The inhibition index of L-leucine was 15 at 20° C., but at 35° C. complete inhibition of growth could not be achieved with an inhibition index of 200, the highest index tested. The inhibition index of L-valine increased four-fold over the *p*H range 6·0–5·2. A mixture of purines and pyrimidines also modified the inhibition index of L-valine. When the components of the mixture were tested individually, the modifying effect was exhibited by two of the purines, guanine and xanthine, as shown in Table 2.

Table 2. Modification of Inhibition Index of L-Valine by Guanine and Xanthine

Inhibition index (L-valine)	5 μmoles						
	None	Adenine	Guanine	Uracil	Thymine	Xanthine	Hypoxanthine
0	40*	40	37	44	41	37	45
2·5	46	42	37	41	44	39	46
5	43	40	34	40	39	37	48
10	43	41	16	40	41	33	49
20	39	20	0	36	38	0	43
40	0	0	0	0	0	0	0

* Figures indicate mgm. dry weight. All flasks contained 0·1 μmole L-phenylalanine.

Mathieson and Catcheside[7] have reported that the growth of a histidine-requiring mutant of *Neurospora crassa* is inhibited by certain amino-acids in combination with lysine or arginine. If, however, the inhibitors were added after two days growth, they had no effect. *E*-5212 exhibited a somewhat similar response to post-inoculation additions of the inhibitory amino-acid, as shown in Table 3. All growth flasks were inoculated at zero time and contained 0·5 μmole of the required amino-acid, L-phenylalanine. The inhibitory amino-acid, L-leucine, was added at the indicated times. It can be seen that by only 8 hr. incubation the mutant was less sensitive to the inhibitory amino-acid. The mutant became increasingly resistant to the inhibitor with time, so that by 18 hr. an inhibition index of 400 was insufficient to inhibit growth completely.

The same effect can be demonstrated by measuring oxygen uptake by the usual manometric methods in a Warburg apparatus. The reaction vessels each contained an equal conidial inoculum and 0·5 μmole of L-phenylalanine in Fries minimal medium. Fifty μmoles of L-leucine was tipped in from the side-arm at the times shown in Fig. 1. By 12 hr., the inhibition was of such a nature that the rate of uptake quickly

Table 3. Effect of Adding Inhibitory Amino-acid Post-inoculation

Inhibition index (L-leucine)	Post-inoculation time (hr.)							
	0	4	8	12	18	25	36	48
0	41*	40	42	41	43	42	41 (9)†	40 (19)†
10	25	34	35	37	34	38	39	43
20	0	0	14	27	29	34	38	40
100	0	0	0	11	20	26	37	37
400	0	0	0	0	14	23	36	33

* Figures indicate mgm. dry weight after 72-hr. growth. All flasks contained 0·5 μmole L-phenylalanine.
† Growth (mgm.) at designated time.

returned to that shown by the cells with no inhibitor present.

The primary result of the single genetic block in *E*-5212 is the requirement of phenylalanine or phenylpyruvate for growth. On further study, however, it has been shown that growth of the mutant on phenylalanine is subject to inhibition by any one of 14 amino-acids[2]. We have demonstrated here that the amino-acid inhibition, and consequently growth of the mutant, is in addition sensitive to a number of environmental variables. It has not yet been determined if the amino-acid inhibitions observed in *E*-5212 are the result of competition for entry into the cell or of competition for an intracellular site. It is suggested, nevertheless, that the site must be of such a nature that its affinity for phenylalanine and the inhibitory amino-acid is subject to the modifying factors discussed here.

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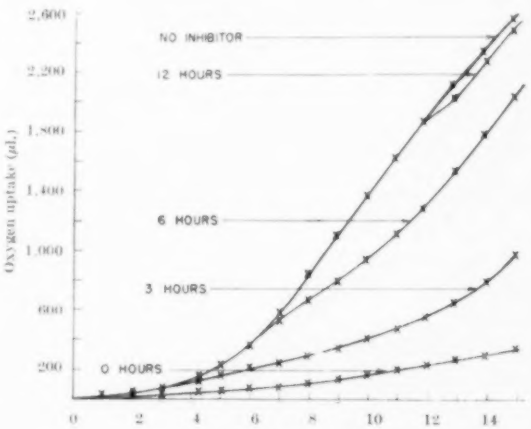

Fig. 1. Effect of inhibitory amino-acid on oxygen uptake. Vessels contained 0·5 μmole L-phenylalanine. 50 μmoles of L-leucine was tipped in at the times indicated

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Response of Japanese Quail to Restricted Lighting

Recent publications on light response of the domestic fowl have directed renewed attention to the fact that a hen's reactions to experimental light stimulation depend, in part, on the conditions prevailing before a given light treatment[1–4]. Short-day lighting of immature pullets may lead to increased rate of egg production immediately following maturation, depending both on the length of pretreatment and light intensities used. Similarly, it has been shown that laying hens held in complete darkness will resume high rates of lay afterwards, even under light intensities considered insufficient when given without a preceding dark period[5]. The work in ref. 5 indicated that short but frequent doses of intense light may over-stimulate hens so that subsequent treatment with continuous light results in reduced rates of lay. A similar experiment with Japanese quail (*Coturnix coturnix japonica*) is reported here, in an effort to establish its usefulness as a pilot animal for the fowl.

Approximately 300 *Coturnix* were reared to 5 weeks of age. They belonged to three closed populations, all derived from the same original stock, but each in their first generation of selection for egg number. Genetically these populations may, therefore, be considered alike. The chicks were brooded in a quail battery and were given weak all-night light from a red 7-W. bulb for the first three weeks. They were then placed in chick batteries under natural daylight. At 5 weeks the birds were sexed and the females moved to single cages with 6 in. × 8 in. floor space; each population was in a separate location. Two of these were windowless chambers equipped with a light-trap at the entrance. The third room, reserved for the control treatment, was located in an open chicken house. Experimental light treatments were first applied at 6 weeks of age when a few hens had already begun to lay eggs.

Group *A*, the control, was given 14 hr. of light every day, at an intensity of more than 1 foot-candle. Group *B* was given no light, except for such light as required when marking egg cards above the cages. This was done by means of a weak pencil flashlight, shielded to avoid direct exposure of the birds to light. Group *C* was given 1 min. of intense light of approximately 2 ft.-c. every hour. These conditions were maintained until the birds were 12 weeks old. At that time the light regimes of groups *B* and *C* were reversed, giving light at the rate of 1 min./hr. to hens preconditioned in darkness and vice versa. No change was made for Group *A*. At 16 weeks the birds were weighed and placed on normal light.

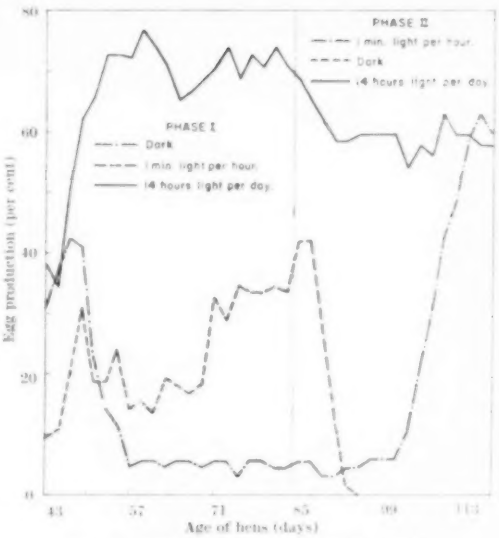

Fig. 1. Dependence of rate of lay on light regime

The response of the hens' rate of egg production to changes in light pattern is shown in Fig. 1. At 6 weeks of age the populations had started to lay at somewhat different rates. The onset of experimental lighting forced most of the hens of Group *B* treated in the dark out of production and prevented those not laying from beginning to do so. Within 2 weeks the rate of production in this group dropped to less than 10 per cent. Similarly, there was some reduction in rate of lay for Group *C* birds under intermittent lighting; after about 2 weeks this population began a consistent rise in lay up to about 40 per cent by the sixth week of treatment.

After the switch of light regimes the two experimental groups changed their egg-laying pattern radically. Group *B*, previously in darkness, showed a rapid rise in egg production 2 weeks after the change to intermittent lighting. Within 4 weeks these hens had reached or exceeded the rate of lay of control birds. In contrast, the group held in darkness following treatment with intense intermittent light stopped egg production completely within a week of change in conditions, and stayed out of lay beyond 16 weeks of age.

In order to reach a general interpretation of these results, one may consider each type of experimental lighting first in its role as direct stimulus and, secondly, in its function in preconditioning the hens for subsequent lay. One may further consider the period of maturation before 6 weeks of age as preconditioning the hens with 14 hr. of light per day.

Viewed in this manner, the results suggest that intermittent lighting stimulates egg production of hens less than 14 hr. of light per day, but more than complete darkness does. It also seems clear that intermittent lighting following dark treatment is much more effective in its stimulatory role than after pretreatment with 14 hr. of light per day. Conversely it would appear that dark treatment

reduced egg production more drastically after hens were preconditioned with intermittent lighting than was the case following the 14 hr. of light a day of the maturation period.

One may conclude that dark treatment of *Coturnix* while almost completely preventing egg production during its application may serve to enhance afterwards the response of hens to light. In contrast, the intermittent light regime permits only sub-optimal productivity unless preceded by a dark period or perhaps other treatment; it has adverse effects on the subsequent ability of hens to lay in darkness, when compared to normal 14 hr. of light per day. These conclusions are in general agreement with results obtained for chickens[1].

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Presence of Blood Antigens in Fish Mucus and its Possible Parasitological Significance

WE have recently shown in this laboratory that each species of fish appears to secrete its own specific mucus[1]. The differences between mucus from various species can be detected by chromatographic methods. With closely related species, like *Sebastes marinus* L. and *S. mentella* Travin, several types of chromatographic technique may be required in order to detect any difference between the two forms of mucus[2]. At present we know very little about the nature of this species specificity of the mucus. Some of the chromatographically separable components fluoresce on exposure to ultra-violet radiation and some are ninhydrin-positive.

Fish serum proteins are, of course, species specific, and therefore we have used some specific anti-fish sera to test for the presence of serum protein components in body and gill mucus. The recently described cellulose acetate membrane immunodiffusion method of Consden and Kohn[3], which we have already shown can be used to distinguish between the closely related *Sebastes* species mentioned[2], was used in this work.

Anti-bass (*Labrax morone* L.) serum *R* 923 was produced by injecting bass serum into a 2-kgm. male albino rabbit by a course of subcutaneous injections according to the following procedure: A preliminary injection of 0·5 ml. bass serum was followed after a week by a second similar one with another three days later and a fourth two days later still. The rabbit was bled out under nembutal, a week after the last injection. The antiserum so produced gave a homologous titre of 1 in 12,000 and a photronreflectometer sigma tau value of 152. Oudin[4] and Ouchterlony[5] immuno-diffusion studies showed that it contained at least six distinct antibodies to the homologous serum. Two of these antibodies reacted with components in *Sebastes marinus* serum and one reacted with cod (*Gadus callarias* L.) serum. No heterologous reaction with coalfish (*Gadus virens* L.) serum was detected. Further studies of bass blood are being reported elsewhere[6].

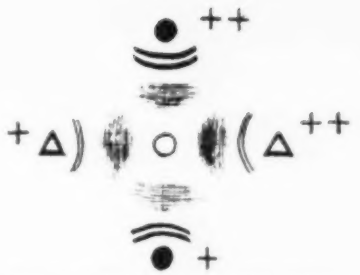

Fig. 1. Diagram of Consden-Kohn reactions between antibass serum *R* 923 (○) and bass mucus (●). Upper and lower reactions are with body mucus and left and right reactions are with gill mucus (△). Plus signs indicate approximate quantities applied. The inner broad bands are nigrosine-positive, the outer lines of precipitation are both ponceau *S*- and nigrosine-positive

When the anti-bass serum *R* 923 was treated with bass mucus using the Consden-Kohn cellulose acetate membrane technique it was found that three antigen antibody (*AnAb*) reactions occurred (Fig. 1). The two outer *AnAb* reactions were detectable by ponceau *S* staining which produced fine clearcut lines of reaction. The more diffuse innermost zone of precipitation was not detectable with ponceau *S*, but required the use of nigrosine staining. It was also found, as can be seen in Fig. 1, that the gill and body mucus reacted somewhat differently. The reactions were stronger with body mucus than with gill mucus. This is perhaps surprising since gill mucus might be more likely to be contaminated with blood than body mucus. It should be pointed out that in the samples studied no contaminating blood was detected. Furthermore, the ponceau *S*-positive *AnAb* reactions were well separated from each other whereas with gill mucus the two lines of precipitate, although discrete, were very close to each other. This would indicate that the relative concentrations of the two antigens involved differ in gill and body mucus.

Anticod serum *R* 712 available from previous work on intragenic relationships in the genus *Gadus*[7] was used to study the body mucus of *Gadus callarias*. Only a single *AnAb* reaction faintly ponceau *S*-positive was found. Subsequent staining with nigrosine gave no further reactions, but the ponceau *S*-positive band stained more strongly.

These results show that some of the serum protein antigens of fishes are also secreted in mucus. These species-specific antigens may be responsible, in part at least, for the ability of certain fish parasites to detect their specific hosts. Wright[8] has pointed out that such parasites must detect their hosts by chemotactic methods, and the presence of species-specific serum proteins in the body mucus suggests a possible basis for this.

Further work is in progress.

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Occurrence of a Species of *Halammohydra* on the Isles of Scilly

DURING the period March 24–28, 1959, collections of the interstitial fauna on several shores of the Isles of Scilly were made. On the very sheltered muddy sand shores of the islands of Tresco and St. Martin's, a small number of specimens of the coelenterate, *Halammohydra* Remane, were recorded, in the surface 5 cm. of sand. The samples were treated with formalin immediately after sampling and this rendered exact identification impossible.

Attempts by one of us (L. A. H.) to collect live specimens at Easter, April 9–23, 1960, were unsuccessful. It may be, therefore, that the earlier presence of the animals was accidental, the true habitat being in the sub-littoral. Alternatively, it may be that these animals exhibit a seasonal cycle and were much less frequent at the time of the 1960 sampling.

The specimens exhibit certain differences from any of the known species, the number of tentacles varying from 9 to 15. Swedmark[1] points out that regional differences occur in the various species.

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Slugs at Low Temperatures

DAMAGE by slugs in gardens and farms is usually worst in late autumn and early spring. There are three reasons for this. First, some species are most numerous in winter[1]. Secondly, alternative foods are scarce, and crop plants such as germinating wheat or the young shoots from delphiniums are sometimes almost the only food available. Thirdly, slugs are active at temperatures which would put most cold-blooded animals into chill-coma.

Experiments have shown that different species of slugs have different chill-coma temperatures. *Agrolimax reticulatus*, which is incidentally a most important pest on farms, is particularly well adapted to life at low temperatures. It is not completely immobilized even at 0° C., and at 0·8° C. moves and feeds apparently normally. *Arion hortensis*, an important garden pest, seldom moves spontaneously or feeds below 5° C. *Milax budapestensis* is intermediate in its temperature relations to the other two species, for it is active at 5° C., but is inactive at 0·8° C.

Some years ago I showed that many insects[2], and also amphibians[3], change their chill-coma temperature by several degrees centigrade within 24 hr. when kept at different temperatures. Similar results for fish, though with a longer period of acclimatization, are well known. I fully expected that slugs would behave similarly.

However, *Agrolimax reticulatus* and *Arion hortensis* do not seem to show any low-temperature acclimatization at all. The chill-coma temperature seems to be quite unaffected if these slugs are kept for from 1 to 10 days at (*a*) 5° C. at (*b*) a temperature fluctuating between 0° C. and 10° C., and at (*c*) a constant temperature of 20° C. The explanation for this difference from insects, fish and amphibians has not been found, but slugs seem well adapted to life at low temperatures and do not readily lose this adaptation. The observations of Dainton[4] that dormant slugs become active, in the laboratory, when the temperature falls, is obviously relevant, but the behaviour of these animals under natural conditions in the field needs much further study.

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Trapped Primary Product of Photosynthesis in Green Plants

BY use of a suitable method of flash photometry five types of absorption changes (types 0, 1, 2*a*, 2*b*, 3) have been observed during photosynthesis in green plant cells. Measurements under various physical and chemical conditions lead to the following assumptions on the related reactions[1].

The absorption change type 1 is caused by a photochemical reaction on chlorophyll Chl a_1. Probably a metastable state of chlorophyll Chl a_1^* ($\tau \approx 5 \times 10^{-5}$ sec.) is formed, which mediates an electron transfer between an electron-donator D and an electron-acceptor A:

$$D(\text{Chl } a_1)A \xrightarrow{h\nu} D(\text{Chl } a_1^*)A \longrightarrow D^+(\text{Chl } a_1)A^- \quad (1)$$

The absorption changes type 2 were first observed by Duysens[2] using a static measuring method with excitation of photosynthesis by steady light; equal absorption changes result from the application of flash photometry[1]. These absorption changes are characterized by two negative maxima ($\sim$ 420 mμ, 475 mμ) and one positive maximum at 515 mμ. The course of the decrease of absorption as a function of wave-length in the neighbourhood of 420 mμ is comparable with the course of an oxidation of cytochrome[2].

Kinetic experiments carried out by flash photometry led to the conclusion that the absorption changes type 2 ($\tau = 10^{-2}$ sec.) are involved in the primary reactions of photosynthesis[1]. Further we succeeded in splitting up the absorption changes type 2 into two reactions, designated as type 2*a* and type 2*b*, by extraction with cold petroleum ether[3,4]. After extraction the absorption changes at 475 mμ and 515 mμ (type 2*b*) disappear, while a negative absorption change with a shift to $\sim$ 425 mμ still can be seen. Due to the absence of type 2*b*, it is possible to detect a small positive absorption change near $\sim$ 530 mμ which is connected with that at $\sim$ 425 mμ (type 2*a*).

The results of our first measurements of absorption changes at low temperatures were reported at a meeting to discuss fast reactions in solution at Hahnenklee[5] (1959). The reaction type 1 (production of Chl a^*) occurs at −150° C. in just the same way as at + 20° C. Therefore an electron transfer according to reaction (1) should also be possible at −150° C. The following observations on type 2*a* give evidence of this fact.

On illumination of spinach chromatophores at −150° C. the absorption changes: type 2*b* (475 mμ and 515 mμ) does not occur. The reaction type 2*a*, however, continues to occur at −150° C. On exposure to light, a decrease in absorption occurs at $\sim$ 425 mμ (Fig. 1). Coupled with this decrease at $\sim$ 425 mμ is a small increase at $\sim$ 530 mμ, coincident with the observations made after extraction with petroleum

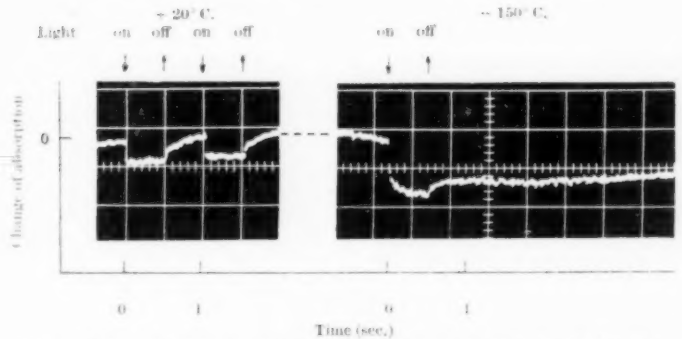

Fig. 1. Changes of absorption at 425 mμ caused by red illumination of chromatophores of spinach

ether. After switching off the light, the absorption changes at ~ 425 mμ and ~ 530 mμ, however, are not reversible at − 150° C., that is, a product is trapped at − 150° C. (Only after thawing to 0° C. does a back reaction occur.) These results show that the trapped product is probably one of the two primary products (D^+ or A^-). The course of the negative absorption change as function of wave-length in the range of 425 mμ suggests that the primary product is probably identical with the oxidized form of a cytochrome ($D^+ = cyt^+$). The small positive change of absorption at ~ 530 mμ, however, normally does not appear on oxidation of cytochromes. It should be emphasized that the experiments have been carried out with material which was photochemically active after the temperature had been raised from − 150° C. to + 20° C. (proof by Hill reaction).

An irreversible oxidation of cytochrome at low temperatures in purple bacteria, especially *Chromatium*, has been already reported by Chance and Nishimura[6].

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Fixation of Nitrogen-15 by Excised Nodules of *Discaria toumatou*

Discaria toumatou (Rhamnaceae) has previously been recorded as a nodulated plant in New Zealand[1]. The nitrogen-fixing ability of its nodules has now been studied experimentally.

In these experiments seedlings of *D. toumatou* made no growth in aerated nutrient solutions lacking added nitrogen whether nodules were present or not. In solutions containing 5 p.p.m. nitrogen as nitrate only, plants that were nodulated grew normally, non-nodulated plants becoming moribund.

Nodulated plants of *Coriaria arborea*, in contrast, made normal growth in aerated nutrient solutions lacking added nitrogen, but became moribund when nodules were absent. Previous work has shown that excised nodules of this plant are able to fix atmospheric nitrogen[2].

Experiments in which excised nodules of *Discaria* were exposed to an atmosphere enriched with nitrogen-15 have also been carried out. Some nodules for these experiments were obtained from plants dug in the field. The roots were washed free of soil and transferred within 2 hr. to flasks containing an aerated nutrient solution lacking added nitrogen. They remained in this solution for two days before nodules were excised and exposed to nitrogen-15. Other nodules were obtained from plants of *Discaria* growing in aerated nutrient solution containing 5 p.p.m. nitrate nitrogen. Excised nodules of *Coriaria arborea* were exposed to nitrogen-15 at the same time. These were obtained from plants growing in aerated nutrient solutions as shown in Table 1.

All nodules were exposed for 40 hr., as previously described[3], to an atmosphere containing 90 per cent nitrogen enriched with 32 atoms per cent excess nitrogen-15. Nitrogen was then extracted with 3*N* hydrochloric acid.

Table 1. ENRICHMENT OF EXCISED NODULES FROM ATMOSPHERE CONTAINING NITROGEN-15

	Nitrogen-15 enrichment (atoms per cent excess)
Discaria from soil	0·10
Discaria from 5 p.p.m. nitrogen solution	0·095
Coriaria from solution lacking nitrogen	> 0·2
Coriaria from 5 p.p.m. nitrogen solution	0·22
Coriaria from 40 p.p.m. nitrogen solution	0·33

These experiments provide evidence that nodules of *Discaria toumatou* are capable of fixing atmospheric nitrogen. Under the conditions employed, however, they differed from those of *Coriaria arborea* in being unable to supply the plant's total need of nitrogen.

In the field *Discaria* grows quite differently from what it does in solutions: it is spiny and almost leafless. One would suppose that this type of growth uses less nitrogen, and it is therefore possible that the nodules can support the growth of *Discaria* in Nature and, perhaps, even that of its usual associates such as sweet briar (*Rosa rubiginosa*).

I am indebted to Mr. T. A. Rafter, director of the Institute of Nuclear Sciences, Department of Scientific and Industrial Research, and Dr. A. D. Campbell, Chemistry Department, University of Otago, for their collaboration in this work, which has been aided by a grant from the University of New Zealand research fund.

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BACTERIOLOGY

Lysogenic Conversion in the Genus *Proteus*

THE presence of prophage renders a bacterial cell immune to homologous bacteriophage. Homologous phage often adsorbs and penetrates the immune cell but does not undergo reduction to prophage and its genetic material is gradually 'diluted out' during multiplication of the cell[1]. Burnet and Lush[2] were the first to encounter a variation of this theme. They studied a lysogenic coccus which did not adsorb the homologous phage. Other workers[3,4] have since described systems in *Salmonella* where the presence of prophage modifies adsorption of homologous or heterologous phage. Changes in properties of bacteria occasioned by the presence of prophage are termed lysogenic conversions[5].

The recovery of a series of temperate phages from lysogenic strains of *Proteus* enabled the study of transduction[6] and conversion in this genus. A series of eleven different phages were employed. Phages 12/57, 49/*F*7, 50/*F*7 and 54/*F*7 were obtained by ultra-violet irradiation of *Proteus* strains 12, 49, 50 and 54, respectively. The indicator organism for the phage obtained from *Proteus* 12 was *Proteus* 57, and the indicator organism for phages from *Proteus* 49, 50 and 54 was *Proteus F*7. Phages 34/13 and 36/13 were present in the supernatant fluids of 10-day broth cultures of *Proteus* 34 and 36, respectively. *Proteus* 13 was the indicator organism for both these phages. Phages $\frac{6}{24}/6$, $\frac{12}{57}/57$, $\frac{14}{20}/14$, $\frac{14}{20}/20$ and $\frac{24}{25}/14$ were present in the supernatant fluids of 10-day broth cultures of *Proteus* strains 6 and 24, 12 and 57, 14 and 20, 14 and 20, 24 and 25, respectively. The indicator organisms for these phages were *Proteus* strains 6, 57, 14, 20 and 14, respectively. Organisms 49, 50 and 54 are *vulgaris* varieties of *Proteus*. The remainder are *mirabilis* strains.

Adsorption experiments of homologous phage to the lysogenic *A* phase[7] wild strains were done by adding 1 ml. of phage suspension to 1 ml. of an aerated overnight broth culture of the organism at a multiplicity of infection of 1. After 20 min. at 37° C. the bacteria were rapidly deposited by centrifuging and the clear supernatant titrated for unadsorbed phage. The 20 min. allowed for adsorption is less than the latent period of any of the phages and more than required for 95 per cent adsorption to indicator strains. Control experiments consisted of 1 ml. of the phage suspension in 1 ml. of broth. These were treated like the tests. Results indicate that only strain 54 adsorbs homologous phage (phage 54/*F*7). In this instance the phage titre of the supernatant was reduced from 1×10^9/ml. (control) to 1×10^6/ml. The remaining 10 phages do not adsorb at all to the corresponding wild lysogenic strains.

The lysogenic *Proteus* were irradiated with ultra-violet light according to the method of Lederberg and Lederberg[8]. Among the survivors of strains 12, 34, 36, 49, 50 and 54 colonies were recovered which are lysed by homologous phage. These sensitive variants are presumably organisms which have been cured of prophage as no phage can be recovered from them. Plaques formed by homologous phage on these sensitive variants have turbid centres due to the growth of lysogenized cells. Cultures of the turbid centres yield organisms with identical phage-adsorbing properties to those of the corresponding wild strain. Prophages present in wild strains 12, 34, 36, 49 and 50 are thus converted in respect of phage-adsorbing capacity. Although non-lysogenic derivatives of the hosts of phages $\frac{6}{24}/6$, $\frac{12}{57}/57$, $\frac{14}{20}/20$, $\frac{14}{20}/14$ and $\frac{24}{25}/14$ have not been obtained it is probable that these prophages exert a similar converting effect. Prophage 54/*F*7 is the exception. Lysogenic immune wild *Proteus* 54 adsorbs phage 54/*F*7 as readily as the sensitive variant.

Phages 12/57 and 34/13 previously used in transduction experiments[6] readily lysogenize most cells of the indicator strains (*Proteus* 57 and 13 respectively) at multiplicities of infection > 5. *Proteus* 57 and 13 lysogenized in this manner and labelled 57(12/57) and 13(34/13) respectively were freed of unadsorbed phage by suspending in the corresponding phage antiserum for 30 min. After centrifuging, the serum was decanted and the deposit streaked on MacConkey agar to yield single colonies. These colonies have the following properties:

(1) Broth cultures of 57(12/57) and 13(34/13) spontaneously liberate phage active on corresponding non-lysogenic strains. These phages are neutralized by antiserum to phages 12/57 and 34/13 respectively.

(2) The strains do not adsorb homologous phage.

(3) They are morphologically identical to strains 57 and 13.

(4) *Proteus* 13(34/13) does not adsorb phages 5 and 25. These phages were isolated from sewage and are active on *Proteus* strains 5 and 25 respectively[9]. *Proteus* 13 is lysed by these phages.

(5) Organisms 57(12/57) and 13(34/13) when matched against 57 and 13 respectively in the *A* phases[7] on nutrient agar show positive Dienes[10] phenomena, that is, they do not swarm into each other and maintain a clear line of demarcation. Fig. 1 illustrates this reaction between strains 57(12/57) and 57. The antigenic differences involved which are responsible for this phenomenon have not yet been identified.

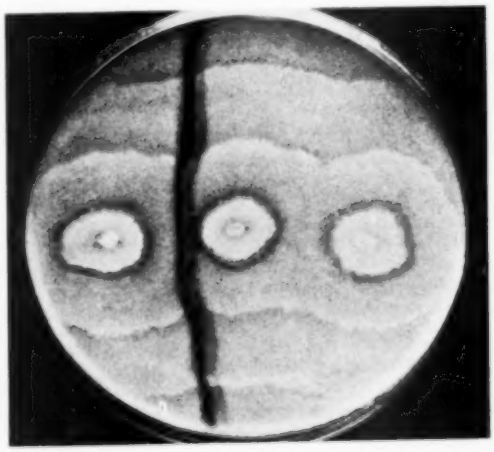

Fig. 1. Nutrient agar plate inoculated at one point on the left with strain 57(12/57) and at two adjacent points with strain 57. Incubated overnight at 37° C. Note how the inocula of strain 57 swarm into each other. The sharp line of demarcation between this spread and the swarming of strain 57(12/57) on the left denotes a positive Dienes phenomenon

Strains 57 and 13 can be transduced to streptomycin resistance by phages 12/57 and 34/13 propagated on streptomycin-resistant mutants of 57 and 13 respectively[8]. Lysogenic transductants possess all the properties of strains lysogenized with non-transducing phage.

Differences in properties of strains 57 and 57(12/57) and strains 13 and 13(34/13) are attributed to the presence of converting prophages 12/57 and 34/13. Conversion is in respect of phage-adsorbing capacity and possibly other antigenic changes as well.

Phages 12/57 and 34/13 are thus competent in transducing and converting systems. A similar position obtains with *Salmonella* phage *P22*. This phage has been extensively used in transduction experiments and can produce lysogenic conversion[4]. A possible difference is that this phage is capable of producing conversion in the vegetative state (phage conversion). No attempt has yet been made to investigate the latter possibility for the *Proteus* phages mentioned.

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Elimination of Transmissible Drug-resistance by Treatment with Acriflavin

The first isolation of multiple resistant *Shigella* was reported by Kitamoto[1]. This was resistant to four drugs (r_4): streptomycin, tetracycline, chloramphenicol and sulphanilamide. *E. coli* r_4 was isolated in the epidemic of *Sh. flexneri* 3*a* r_4 (refs. 2 and 3). *Sh. flexneri* 2*a* r_3 and *E. coli* r_3 were also isolated in another epidemic, which were resistant to streptomycin, chloramphenicol and sulphanilamide[4]. *Citrobacter* r_4 and *E. coli* r_4 were isolated from a dysenteric patient after treatment with chloramphenicol[5].

From the epidemiological investigation of the multiple resistant *Escherichia* in the faeces of human beings[6], we have learned more about the multiple resistant *Shigella* and the general phenomena among Enterobacteriaceae.

Ochiai[7] and Akiba[8] reported that the multiple resistance was transmitted between *Shigella* and *E. coli* following mixed cultivation. This transmission is not mediated by transduction, transformation or filtrable agent, but by cell-to-cell contact[9,10] without regard to the polarity of *F* factor[11]. It has also been shown that the multiple resistance is transmitted between every genera of Enterobacteriaceae[12], whereas perhaps only 3–5 per cent of the strains of *Escherichia* would have given positive results in bacterial recombination.

Artificial elimination of the transmissible drug-resistance by treatment with acriflavin was carried out by Hirota's method[13].

The drug-resistant cells were inoculated into Difco brain-heart infusion broth containing sublethal concentrations of acriflavin (20 μgm./ml. for *E. coli* and 10 μgm./ml. for *Shigella*). After overnight incubation at 37° C., the cells were streaked on Drigalski's medium and the drug-resistance of each colony was tested. Heart infusion agar was used for assaying resistance to streptomycin, chloramphenicol and tetracycline. For assaying sulphanilamide resistance, semi-synthetic medium was used. It consists of 1 litre of medium *A* (ref. 14) agar enriched with 2·0 gm. casamino-acid, 10 mgm. tryptophan, 2 mgm. nicotinic acid, 10 mgm. thiamin hydrochloride and 2 gm. glucose. The results are shown in Table 1.

Table 1. Frequency of Elimination of Drug-Resistance by Treatment with Acriflavin

Micro-organisms	With acriflavin treatment	Without acriflavin treatment
E. coli O-26 r_4	5/579 (0·9 %)	0/1,580*
,, r_3	15/547 (2·9 %)	0/881
,, r_1	0/579	0/364
Sh. flexneri 3*a* r_4	241/517 (46·6 %)	0/1,198
,, r_3	0/375	0/1,177
,, r_1	201/583 (36·2 %)	0/1,116

r_4, resistant to streptomycin, chloramphenicol, tetracycline and sulphanilamide; r_3, resistant to streptomycin, tetracycline and sulphanilamide; r_1, resistant to tetracycline.
* Numerator, number of the drug-sensitive colony; denominator, number of the total colonies tested.

The drug-resistance of both *Escherichia* and *Shigella* were eliminated from the drug-resistant cells after treatment with acriflavin, and the frequency of elimination of the drug-resistance was higher in *Shigella* than in *Escherichia*. This fact is in agreement with the finding that the loss of the drug-resistance with *Shigella* was more frequent than with *Escherichia* after 6 months storage in cooked meat media. It was also found that all markers for drug-resistance were lost by treatment with acriflavin and the cells became sensitive to all drugs. The drug-sensitive cells thus obtained were not able to transmit the drug-resistance by mixed cultivation with other drug-sensitive cells.

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GENETICS

Structural Mutations

THE premise that linear and continuous sequences of nucleotides in the genetic material (deoxyribonucleic acid (DNA) in most organisms, ribonucleic acid (RNA) in some viruses) specify corresponding linear and continuous sequences of amino-acids in the proteins, that is, the gene products of these organisms, is so fundamental to present-day thinking in the field of molecular biology that it has rightfully been referred to as the 'central dogma'[1,2]. Another premise, inherent in this dogma, is the principle of colinearity of the genetic map with the nucleotide sequence and the definition of a mutation as an alteration in this sequence giving rise in turn to an altered structure in the product proteins. The conclusion has therefore been implicit that every mutation must necessarily result in some alteration in a gene product.

It is the purpose of this communication to point out that this syllogism is neither logically sound nor necessarily reflective of the situation existing in Nature even on the basis of the fragmentary evidence at present available. It is conceivable that there exist regions in the genetic nucleic acid primarily concerned in the specification not of gene products but with nucleic acid structure itself. The structure here referred to is a 'tertiary' folding or other configurational alteration superimposed on the 'secondary' structure (the hydrogen-bonded helix). That such folding must exist in native genetic material is self-evident from a consideration of the dimensions of the heads of bacteriophages *T2* or *T4* (95×65 mμ)[3], as contrasted with those of the DNA contained therein were it to assume the fully extended, rigid, configuration demanded by the Watson–Crick hypothesis ($6{\cdot}3 \times 10^4$ mμ × 2 mμ). We[4,5] and others[6,7] have speculated that the secondary constituents associated with the DNA of these phages (internal protein(s)[7,8], polyamines[8,9]) may be concerned with the attainment and/or maintenance of this tertiary structure. The hypothesis of scattered regions concerned with tertiary structure has, however, other important consequences which can be tested.

It may be fruitful, for example, to institute a search for phage mutants, which possess *solely* an altered DNA, as a consequence of which they differ in their tertiary structure and in their DNA-protein interaction without, however, any significant alteration in the primary structure of any of the individual proteins specified by this DNA. It is possible that in *T2* and/or *T4* at least such mutations may already have been reported. One such might be the well-known class of acridine-resistant mutants[10,11]. On the basis of work by others[6,12–15] and investigations now in progress in our laboratories, it is likely that, in the dark under carefully controlled conditions, acridines in general and proflavine in particular exert a very specific inhibitory action on phage reproduction. This action occurs during that stage of maturation which is concerned with the integration of previously synthesized, structurally intact, and fully functional DNA with the structural phage proteins, mainly those of the head. The dye has no effect on the elaboration of either DNA (refs. 6, 15) or proteins[14,15] separately. The inhibitory effect may find its cause in the formation of a relatively strong and specific complex between the dye and phage DNA which is, however, rapidly and reversibly dissociated by dilution in the presence of normal phage constituents. Four predictions can then be made: (1) that a one-step proflavine-resistant mutant should be one possessing an altered DNA but normal proteins which allows maturation to proceed at concentrations of dye completely inhibitory to the wild type; (2) that it should be possible to detect this alteration in the DNA by comparing interactions of dye and DNA's from wild-type and mutant respectively by appropriate physical and chemical techniques, while phage proteins isolated from mutant and wild type should be identical in structure and indistinguishable by all criteria; (3) that a relatively large number of different mutants of this type should be isolatable and that these markers should be distributed more or less at random along the full length of the phage genome; (4) that multi-step mutants, which are resistant to higher levels of dyes, should manifest enhanced resistance by the criteria enumerated under (1) and (2).

Prediction (3) brings to mind another class of mutants. The *ht* (extended host range, turbid) markers studied and mapped very carefully by Baylor and her collaborators[16] appear to possess just such a distribution. Yet recent genetic and immunochemical work by Streisinger[17] and structural investigations by Williams and Fraser[18] make it apparent that, phenotypically, host-range and attachment to cells are manifested through just one species of protein, that of the tail fibres[19]. Once again those mutations may control not the structure of a protein *per se* but only that of the nucleic acid itself: in turn this structural alteration controls the interaction of the DNA with some protein(s), itself specified by quite a different section of the genome. Indications of this may be provided by Baylor's recent work on the stepwise and additive nature of these *ht* mutations with respect to their stability to incubation in buffer (Baylor, M. B., private communication).

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, March 20

INSTITUTION OF ELECTRICAL ENGINEERS, LONDON GRADUATE AND STUDENT SECTION (joint meeting with the Utilization Section, at Savoy Place, London, W.C.2), at 6 p.m.—Mr. P. J. H. Rata: "Aluminium in Electrical Engineering"; Mr. A. D. Swanston and Mr. B. W. Towell: "Diesel Railway Locomotives"; Mr. T. E. S. Rickard: "Automatic Programmes for Hot Reversing Mills".

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 6 p.m.—Miss Margaret F. Harker: "Photography in Education" (Cantor Lecture).

INSTITUTE OF METAL FINISHING (at Northampton College of Technology, St. John Street, London, E.C.1), at 6.15 p.m.—Mr. C. F. Marx and Mr. D. Povey: "Zinc Plating from the Pyrophosphate Bath".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the Ewell County Technical College Faraday Society, at the Ewell County Technical College, Reigate Road, Ewell, Surrey), at 7 p.m.—Dr. R. N. Hazeldine: "The Chemistry of Fluorine".

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Sir William Holford: "Birth of a City".

Monday, March 20—Tuesday, March 21

SOCIETY OF CHEMICAL INDUSTRY, PESTICIDES GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 10 a.m. daily—Symposium on "Fungicides in Agriculture and Horticulture".

Tuesday, March 21

INSTITUTION OF CHEMICAL ENGINEERS (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Discussion meeting on: "Some Factors in the Safe Operation of Air Separation Plants".

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Discussion on "Self-Adaptive Control Systems" opened by Dr. J. H. Westcott, Dr. J. L. Ponce, Dr. P. E. W. Grinsted and Mr. P. H. Hammond.

UNIVERSITY OF LONDON (at the Senate House, University of London, W.C.1), at 5.30 p.m.—Prof. W. Z. Hassid (University of California): "Transformation of Carbohydrates in Plants".*

UNIVERSITY OF LONDON (in the Gustave Tuck Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. D. A. Wright: "Thermoelectric Generation".* (Last of five lectures on "Generation of Electricity without the use of Rotating Machinery".)

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place, London, W.1), at 7 p.m.—Mr. G. H. Lee: "Some Aspects of Buffeting".

Tuesday, March 21—Thursday, March 23

INSTITUTE OF METALS (at Church House, Great Smith Street, London, S.W.1), at 10 a.m. daily—Spring Meeting.

Wednesday, March 22

INSTITUTE OF PHYSICS AND THE PHYSICAL SOCIETY, COLOUR GROUP (in the Lecture Theatre of the British Lighting Council, Lancaster Place, London, W.C.2), at 3 p.m.—Mr. H. L. Gloag: "Some Principles of Good Colour in Buildings"; Mr. D. L. Medd: "Influences on the Use of Colour in Building in the United States of America".

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Prof. F. Hodson and Dr. G. C. Lewarne: "A Mid-Carboniferous (Namurian) Basin in Parts of the Counties of Limerick and Clare, Ireland".

BRITISH INSTITUTION OF RADIO ENGINEERS, COMPUTER GROUP (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Discussion on "The Future of High Speed Storage Systems".

INSTITUTE OF FUEL (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 5.30 p.m.—Mr. E. Holmes-Smith, Mr. J. Lister and Mr. P. V. Liddell: "The New Wilton High-Pressure Cyclone Boiler".*

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND SUPPLY SECTIONS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. R. Carruthers and Mr. D. L. Smart: "The Engineering Aspects of Plasma Physics".

INSTITUTION OF MECHANICAL ENGINEERS (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Sir Frederick Bartlett: "The Bearing of Psychology and Medicine upon Engineering" (James Clayton Lecture).

SOCIETY OF CHEMICAL INDUSTRY, FOOD GROUP (at 14 Belgrave Square, London, S.W.1), at 6.15 p.m.—Mr. J. Mauron: "Control of the Nutritional Qualities of Milk Protein".

Thursday, March 23

LINNEAN SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Monsieur J. Prevost: "French Biological Work in the Region of Isle Kerguelen".

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place, London, W.1), at 6 p.m.—General H. Ziegler: "Problems of Short Take-off and Landing". (Fourteenth Louis Bleriot Memorial Lecture.)

OIL AND COLOUR CHEMISTS' ASSOCIATION (at the Royal Society of Tropical Medicine and Hygiene, Manson House, 26 Portland Place, London, W.1), at 7 p.m.—Mr. H. C. Shellard: "Can the Climatologist Help You?"

Friday, March 24

ROYAL ASTRONOMICAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.15 p.m.—Geophysical Discussion on "Geodetic Uses of Artificial Satellites". Chairman: Dr. A. H. Cook. Speakers: Brigadier G. Bomford, Dr. R. d'E. Atkinson, Dr. A. P. Willmore and Mr. W. H. Guier.*

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT LECTURER IN PHYSICS—The Registrar, Queen Mary College (University of London), Mile End Road, London, E.1 (March 25).

ASSISTANT LECTURER (trained in electron microscope techniques) IN BIOPHYSICS in the Faculty of Medicine—The Registrar, The University, Manchester 13 (March 25).

PRINCIPAL (graduate of a British university, responsible experience in technical education, and preferably some industrial experience) OF THE FROME TECHNICAL INSTITUTE—Chief Education Officer, County Education Office, Trull Road, Taunton, Somerset (March 30).

HEAD OF THE DEPARTMENT OF MATHEMATICS—The Principal, Northampton College, St. John Street, London, E.C.1 (March 31).

IMPERIAL CHEMICAL INDUSTRIES FELLOWS (preferably with the degree of Ph.D. or equivalent research experience) to carry out original research in chemistry or physics, for a period not exceeding three years—The Registrar, University College of North Staffordshire, Keele, Staffs (March 31).

ASSISTANT LECTURER or LECTURER (preferably with an honours degree in mathematics) for work at the University Tidal Institute and Observatory—The Registrar, The University, Liverpool (April 4).

ASSISTANT LECTURER or LECTURER (with an honours degree in physical oceanography or physics, and prepared to spend several weeks each year at sea) IN THE DEPARTMENT OF OCEANOGRAPHY—The Registrar, The University, Liverpool (April 4).

LECTURER or ASSISTANT LECTURER IN BIOCHEMISTRY—The Registrar, The University, Leeds (April 4).

LECTURER (with a good honours degree, teaching experience up to degree level, and research experience) IN ZOOLOGY at the Nigerian College of Arts, Science and Technology, Zaria Branch—The Council for Overseas Colleges, 12 Lincoln's Inn Fields, London, W.C.2 (April 7).

RESEARCH BIOCHEMIST (with postgraduate research experience in the fields of protein chemistry or nutrition), to join a team investigating the effects of heat treatment on nutritional availability of the amino-acids in the proteins of foods—The Secretary, School of Agriculture, The University, Downing Street, Cambridge (April 7).

SENIOR LECTURER IN PHARMACY in the Science Department, Jamaica College of Arts, Science and Technology, Kingston—The Council for Overseas Colleges, 12 Lincoln's Inn Fields, London, W.C.2 (April 7).

LECTURER (with special qualifications in Latin American geography) IN GEOGRAPHY—The Registrar, The University, Leicester (April 8).

CHAIR OF PHYSICS—The Registrar, The University, Sheffield (April 15).

ASSISTANT LECTURER (with an honours degree in mathematics and preferably an interest in numerical analysis) IN MATHEMATICS—The Registrar, King's College (University of London), Strand, London, W.C.2 (April 17).

READER IN PHYSIOLOGY at London Hospital Medical College—The Academic Registrar, University of London, Senate House, London, W.C.1 (April 17).

LECTURER IN PHYSICS at the University of New England, Armidale, New South Wales, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, April 30).

LECTURER IN THE DEPARTMENT OF PHYSIOLOGY at Makerere University College, East Africa—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (April 30).

SENIOR LECTURER IN PHILOSOPHY at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, April 30).

UNIVERSITY ASSISTANT LECTURER IN ARCHÆOLOGY to give instruction in the archæology of the Anglo-Saxon and Celtic peoples—The Secretary of the Appointments Committee, Faculty of Archæology and Anthropology, Downing Street, Cambridge (May 15).

ASSISTANT OR ASSOCIATE PROFESSOR (with a Ph.D. and teaching experience) IN PHARMACOLOGY—Dr. H. G. Downie, Professor and Head, Department of Physiological Sciences, Ontario Veterinary College, Guelph, Ontario, Canada.

HEAD (physical chemist with outstanding qualifications and experience, and an original outlook) OF THE PHYSICO CHEMICAL DIVISION, to direct basic studies into the bulk properties of polymers and to initiate research in his own field of interest—The Director, Arthur D. Little Research Institute, Inveresk, Musselburgh, Midlothian.

LECTURER IN PHYSICS—The Clerk to the Governors, Northern Polytechnic, Holloway, London, N.7.

SENIOR TECHNICIAN (with experience in a physiological laboratory) to assist in work on lung function—The Secretary, Institute of Child Health, The Hospital for Sick Children, Great Ormond Street, London, W.C.1.

UNION CARBIDE POSTDOCTORAL FELLOW IN ORGANIC CHEMISTRY—Prof. R. C. Cookson, The University, Southampton.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

General Register Office. Studies on Medical and Population Subjects, No. 16: Area of Residence of Mental Hospital Patients—Admissions to Mental Hospitals in England and Wales in 1957 according to Area of Residence, Diagnosis, Sex and Age. Pp. iv+177. (London: H.M. Stationery Office, 1960.) 15*s.* 6*d.* net. [1312

Department of Scientific and Industrial Research. The Human Implications of Work Study—The Case of Pakitt, Ltd. By Stuart Dalziel and Lisl Klein. Pp. xiii+81. (Stevenage: Human Sciences Unit, D.S.I.R., Warren Springs Laboratory, 1960.) [1312

Manchester Literary and Philosophical Society. Memoirs and Proceedings, Vol. 102, 1959-60. Pp. 81+xiii. (Manchester: Manchester Literary and Philosophical Society, 1960.) 31*s.* 6*d.* [1312

Hatfield Technical College. Eighth Annual Report, Session 1959-60. Pp. 44. (Hatfield: Hatfield Technical College, 1960.) [1312

Biology, Psychology and Belief. By Dr. W. H. Thorpe. (The Fourteenth Arthur Stanley Eddington Memorial Lecture, 3 November 1960.) Pp. 60. (Cambridge: At the University Press, 1961.) 4*s.* 6*d.* net. [1312

Air Ministry: Meteorological Office. British Rainfall 1957: Report on the Distribution of Rain in Space and Time over Great Britain and Northern Ireland during the year 1957 as recorded by about 5,000 Observers. (Ninety-seventh Annual Volume). Pp. iv+245. (M.O. 663). (London: H.M. Stationery Office, 1960.) 32*s.* 6*d.* net. [1312

Government of Northern Ireland: Ministry of Agriculture. Leaflet No. 83: Management and Feeding of Poultry Breeding Stock. Pp. 11. (Belfast: Ministry of Agriculture, 1960.) [1312

Proceedings of the Royal Irish Academy. Vol. 61, Section A, No. 1: The Absolute Convergence of Certain Lacunary Fourier Series. By Siobhan O'Shea. Pp. 1-8. 1*s.* 6*d.* Vol. 61, Section B, No. 7: A Study of the Caudal Gills of Dragonfly Larvae of the Sub-order Zygoptera. By Niall MacNeill. Pp. 115-140+plates 5-9. 5*s.* Vol. 61, Section B, No. 8: The Relationships of some Bog Communities in Western Galway. By D. J. Boatman. Pp. 141-166+plates 10 and 11. 4*s.* 6*d.* Vol. 61, Section B, No. 9: Observations of the Serum Proteins of the Bass *Morone labrax* (L.) (Pisces: Serranidae). By Fergus J. O'Rourke. Pp. 167-176. 1*s.* 6*d.* Vol. 61, Section B, No. 10: The Dragonflies of the Gearagh, West Cork. By Ann Hewitson and Fergus J. O'Rourke. Pp. 177-185. 1*s.* (Dublin: Hodges, Figgis and Co., Ltd., 1960.) [1312

Tube Investments, Ltd. This is T.I. Today. Pp. 16. (London: Tube Investments, Ltd., 1960.) [1312

Planning, Vol. 26, No. 447 (12 December 1960): Community Mental Health Services. Pp. 337-356. (London: Political and Economic Planning, 1960.) 2*s.* 6*d.* [1312

Ministry of Aviation. Reports on Plastics in the Tropics No. 13: Polystyrene Mouldings. Pp. 42. (London: H.M. Stationery Office, 1960.) 5*s.* net. [1312

The Nature Conservancy. Report of the Nature Conservancy for the year ended 30th September 1960. Pp. vii+138+14 plates. (London: H.M. Stationery Office, 1960.) 6*s.* 6*d.* net. [1312

Imperial College of Science and Technology (University of London). Fifty-third Annual Report of the Governing Body, 1959-1960. Pp. iv+123. (London: Imperial College of Science and Technology, 1960.) [1312

The Institute of Physics and the Physical Society. Handbook of Scientific Instruments and Apparatus, 1961 Exhibition. (Advertisement Section for Exhibition Handbook.) Pp. 75. (London: Institute of Physics and Physical Society, 1960.) [1312

Contemporary Psychology and Christian Belief and Experience. By Prof. Malcolm A. Jeeves. Pp. 16. (London: The Tyndale Press, 1960. Published for the Research Scientists' Christian Fellowship.) 1*s.* 6*d.* [1312

National Park Guides, No. 3: Peak District. Pp. viii+90+26 plates. (London: H.M. Stationery Office, 1960.) 5*s.* net. [1312

Proceedings of the University of Durham Philosophical Society. Vol. 13, Series A (Science). No. 14: Soils and Deposits in the Durham Area. 1: Fluvioglacial Soils. By S. G. Willimott and D. W. Gilchrist Shirlaw. Pp. 133-147. No. 15: Soils and Deposits in the Durham Area. 2: Alluvial Deposits. By D. W. Gilchrist Shirlaw and S. G. Willimott. Pp. 148-160. Vol. 1, Series B (Arts), No. 4: The Continental Background of Early Anglian Literature. By F. Norman. Pp. 26-41. No. 5: Sub-Rectangular Earthworks in Germany. By P. Salway. Pp. 42-48. No. 6: Pleremics. By Jens Holt. Pp. 49-53. (Durham: University of Durham Philosophical Society, 1960.) [1512

Other Countries

Annals of the Natal Museum, Vol. 15, Part 2: Terrestrial Isopoda from the Transvaal. By K. H. Barnard. Pp. 45-55. 7*s.* net. Vol. 15, Part 3: Additional Notes on the South African Acrocerid Fauna, with descriptions of New Species of *Acrocera* Meigen and *Psilodera* Gray (Diptera). By Evert I. Schlinger. Pp. 57-67. 7*s.* net. Vol. 15, Part 4: Un Henicocephalide Myrmécophile de l'Afrique Australe: *Compadreres stuckenbergi* n. sp. (Hemoptera). Par André Villiers. Pp. 69-70. 4*s.* Vol. 15, Part 5: A Genus and Species of Wingless Fly from South Africa (Diptera, Sphaeroceridae). By O. W. Richards. Pp. 71-73. 4*s.* 6*d.* net. Vol. 15, Part 6: A New Genus and Species of Sciaridae (Diptera, Nematocera) from South Africa. By Paul Freeman. Pp. 75-77. 4*s.* 6*d.* net. Vol. 15, Part 7: Aculeate Hymenoptera from the Drakensberg Mountains, Natal. By G. Arnold. Pp. 79-87. 6*s.* 6*d.* net. Vol. 15, Part 8: A New Species of Trigonia from the Sundays River Beds of the Uitenhage Series, Cape Province. By Dr. J. A. Pringle. Pp. 89-92+1 plate. 6*s.* 6*d.* net. (Pietermaritzburg: Natal Museum, 1960.) [1312

Publications de l'Institut National pour l'Étude Agronomique du Congo. Carte des Sols et de la Végétation du Congo et du Ruanda-Urundi. 14, -Uele. A, -Sols. C, -Utilisation des Sols. Notice Explicative de la Carte des Sols. Par R. Frankart. Pp. 128. 15, -Kasai. A, -Sols. B, Végétation. Notice Explicative de la Carte des Sols. Par P. Gilson et L. Liben. Pp. 76. (Bruxelles: Institut National pour l'Étude Agronomique du Congo, 1960.) [1312

Colony of Mauritius. Annual Report of the Meteorological Department, 1959. Pp. ii+16. 25 cents. Meteorological Observations and Climatological Summaries, 1959. January. Pp. ii+10. February. Pp. 10. March. Pp. 10. April. Pp. 11. May. Pp. 11. June. Pp. 11. July. Pp. 11. August. Pp. 11. September. Pp. 11. October. Pp. 11. November. Pp. 11. December. Pp. 17. (Port Louis: Government Printer, 1960.) [1312

University of Natal. Wattle Research Institute (South African Wattle Growers' Union—University of Natal—Union Department of Forestry). Report for 1959-1960 (Thirteenth Year). Pp. 48. (Pietermaritzburg: University of Natal, 1960.) [1312

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Organization for European Economic Co-operation: European Nuclear Energy Agency. Convention on Third Party Liability in the Field of Nuclear Energy, Paris, 29th July, 1960. Pp. 67. (Paris: O.E.E.C., European Nuclear Energy Agency, 1960.) [2012

United States Department of the Interior: Fish and Wildlife Service. Fishery Bulletin No. 175: Synopsis of Strigeoidea (Trematoda) of Fishes and their Life Cycles. By Glenn L. Hoffman. Pp. iv+439–469. 30 cents. Fishery Bulletin 186: Sonic Tracking of Adult Salmon at Bonneville Dam, 1957. By James H. Johnson. Pp. iv+471–485. 20 cents. Fishery Bulletin No. 177: Abundance and Life History of Shad, St. John's River, Florida. By Charles H. Walburg. Pp. iv+487-501. 20 cents. (Washington, D.C.: Printing Office, 1960.) [2012

Eastern Nigeria. Annual Report of the Forest Division, 1959-60. Pp. 39. (Enugu: Government Printer, 1960.) 1*s.* 9*d.* net. [2012

Bulletin of the American Museum of Natural History, Vol. 120 Article 2: A Revision of the Genus *Diplotaxis* (Coleoptera, Scarabaeidae, Melolonthinae), Part 2. By Patricia Vaurie. Pp. 161-434. 5.50 dollars. Vol. 12, Article 1: The Ecology and Migrations of Sea Turtles, 4: The Green Turtle in the Caribbean Sea. By Archie Carr and Larry Ogren. Pp. 1-48+plates 1-7. 1 dollar. Vol. 121, Article 2: The Birds of Finca "La Selva", Costa Rica: a Tropical Wet Forest Locality. By Paul Slud. Pp. 49-148+plates 8-26. 2.75 dollars. (New York: American Museum of Natural History, 1960.) [2012

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University of California Publications in Geological Sciences. Vol. 36, No. 8: Multivariate Analysis of Pleistocene and Recent Coyotes (*Canis latrans*) from California. By Eugene Giles. Pp. 369-390. 75 cents. Vol. 39, No. 1: Late Pliocene Floras East of the Sierra Nevada. By Daniel I. Axelrod and William S. Ting. Pp. 1-118 (plates 1-24). 2.50 dollars. (Berkeley and Los Angeles: University of California Press; London: Cambridge University Press, 1960.) [2012

The University College, Ibadan. Calendar, 1960-61. Pp. 101. (Ibadan: The University College, 1960.) [2012

National Academy of Sciences—National Research Council. Nuclear Science Series, Report No. 27 (rev. 1): Source Material for Radiochemistry. Pp. iii+39. (Publication 825). (Washington, D.C.: National Academy of Sciences—National Research Council, 1960.) [2012

A Collection of Papers of the Rational Theory, Book 2. By F. Harrison Stamper. Pp. 10. (Los Angeles: F. Harrison Stamper, 1990 Barnett Road, 1960.) [2012

Centro Brasileiro de Pesquisas Fisicas. Notas de Fisica. Vol. 6, No. 8: The Reactions ^{27}Al (p, p^1) ^{27}al and ^{27}al (a, p) ^{30}Si. By P. D. Forsyth, A. A. Jaffe, I. J. Taylor and F. de S. Barros. Pp. 201-216. Vol. 6, No. 9: Photon Monochromators. By J. Goldemberg and A. O. Hanson. Pp. 217-250. Vol. 6, No. 10: Observation of a Short-Lived Cosmic-Ray Solar Flare Increase with a High-Counting-Rate Meson Detector. By K. G. McCraken and R. A. R. Palmeira. Pp. 251-257. Vol. 6, No. 11: North-South Anisotropy and Anticipatory Increase of Intensity Associated with the Cosmic Ray Storm of February 11, 1958. By Dr. V. Sarabhai and R. Palmeira. Pp. 259-272. (Rio de Janeiro: Centro Brasileiro de Pesquisas Fisicas, 1960.) [2012

Smithsonian Institution, Washington, D.C. United States National Museum Bulletin No. 219: The National Watercraft Collection. By Howard I. Chapelle. Pp. xi+327. (Washington, D.C.: Government Printing Office, 1960.) 3.50 dollars. [2012

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Applications are invited for the posts of Research Officers in Agronomy, Entomology, Plant Pathology, Botany, Soil Chemistry, Agricultural Engineering, Plant Breeding and Statistics in the Agricultural Research Division, Department of Agriculture, Republic of the Sudan. Applicants must possess first- or second-class honours degree with at least two years postgraduate experience. Selected Officer would be expected to conduct research of practical importance). Up to five years contract renewable to a further term. Salary range £S.1,675 by £S.75 annual increments to £S.1,675 with a bonus of one month's salary for each year's service or £S.1,146 by £S.80 to £S.1,786 without bonus (point of entry into scale depending upon qualifications, age and experience). Higher starting or maximum rates can be considered on merit. A cost of living allowance at variable rates over and above basic salary. Unfurnished house would be provided at reduced rent. Furniture can be obtained on hire at reasonable charge. Overseas Leave at the rate of 80 days for each year of service on full pay with free return air passage for officer, wife and up to three children may be taken on completion of 18 months service, thereafter in every calendar year. Those joining the service before June 30 in any one year would be entitled to this leave any time in the year following. No income tax is payable at present.

Applications, giving full details of qualifications, experience and references, should be forwarded to the Sudan Embassy, Appointments Section, 3 Cleveland Row, St. James's, London, S.W.1. Closing date, March 31, 1961.

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REPUBLIC OF THE SUDAN

Applications are invited for the posts of Senior Research Officers to take charge of research Substations in the Agricultural Research Division, Department of Agriculture, Republic of the Sudan. Applicants must possess first- or second-class honours degree with at least two years postgraduate experience. Selected Officers would be expected to conduct research of practical importance and to train and lead a team of Scientists in various research lines. Up to five years contract renewable to a further term. Salary range £S.2,050 by £S.75 to £S.2,125 by £S.85 to £S.2,210 with a bonus of one month's salary for each year's service or £S.2,180 by £S.80 to £E.2,260 by £S.100 to £S.2,360 without bonus (point of entry into scale depending upon qualifications, age and experience). Higher starting or maximum rates can be considered on merit. A cost of living allowance at variable rates over and above basic salary. Unfurnished house would be provided at reduced rent. Furniture can be obtained on hire at reasonable charge. Overseas leave at the rate of 80 days for each year of service on full pay with free return air passages for Senior Officer, wife and up to three children may be taken on completion of 18 months service; thereafter in every calendar year. Those joining the service before June 30 in any one year would be entitled to this leave at any time in the following year. No income tax is payable at present.

Applications, giving full details of qualifications, experience and references, should be forwarded to the Sudan Embassy, Appointments Section, 3 Cleveland Row, St. James's, London, S.W.1. Closing date, March 31, 1961.

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REPUBLIC OF THE SUDAN

Applications are invited for the posts of Senior Research Officers in Agronomy, Plant Physiology, Entomology, Plant Pathology and Plant Breeding in the Agricultural Research Division, Department of Agriculture, Republic of the Sudan. Applicants must possess first- or second-class honours degree with at least two years postgraduate experience. Selected Officers would be expected to conduct research of practical importance, and to train and lead younger Scientists. Up to five years contract renewable to a further term. Salary range £S.1,750 by £S.75 to £S.1,975 with a bonus of one month's salary for each year's service or £S.1,866 by £S.80 to £S.2,106 without bonus (point of entry into scale depending upon qualifications, age and experience). Higher starting or maximum rates can be considered on merit. A cost of living allowance at variable rates over and above basic salary. Unfurnished house would be provided at reduced rent. Furniture can be obtained on hire at reasonable charge. Overseas leave at the rate of 80 days for each year of service on full pay with free return air passages for Senior Officer, wife and up to three children may be taken on completion of 18 months' service; thereafter in every calendar year. Those joining the service before June 30 in any year would be entitled to this leave any time in the following year. No income tax is payable at present.

Applications, giving full details of qualifications, experience and references, should be forwarded to the Sudan Embassy, Appointments Section, 3 Cleveland Row, St. James's, London, S.W.1. Closing date, March 31, 1961.

ROYAL NAVAL SCIENTIFIC SERVICE

GOVERNMENT COMMUNICATIONS HEADQUARTERS

Require Experimental Officers and Assistant Experimental Officers at Government Communications Headquarters, Cheltenham, Glos. Duties widely distributed in field of communications research and development including radio equipment (over wide range of frequency) terminal equipment, aerials, and radio range-finding and direction-finding systems. Propagation studies and experiments carried out. Work also includes data processing, programming and engineering, applications of electronic computing techniques and numerous problems in instrumentation. Candidates must normally be natural born British subjects and of British parentage. Experimental Officers, minimum age 26 and normally under 31. Assistant Experimental Officers, at least 18 and normally under 28. Qualifications should include H.S.C. or G.C.E. (with at least two "A" level subjects) or equivalent, or H.N.C., a University degree or Diploma in Technology. Salaries: Experimental Officer, £1,087 to £1,336; Assistant Experimental Officer, £458 (at 18) to £801 (at 26 or over) to £983. Facilities for further education. Promotion prospects. Appointments unestablished, but opportunities exist for establishment.

Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting Ref. A87/1A.

FELLOWSHIPS FOR RESEARCH IN ELECTROCHEMISTRY

A number of Fellowships for Graduate Students are being offered by the Electrochemistry Research Group of the Chemistry Department at the University of Pennsylvania. They are open to competition from students who can produce evidence of exceptional ability such as a first-class honours degree in physics, chemistry or metallurgy. Research work will be selected from the following fields: electrode kinetics, semiconductor-electrolyte interface, structure of molten electrolytes, and adsorption at the metal-electrolyte interface. Travel costs to and from Philadelphia will be paid for successful applicants. The research work will be suitable to form the basis of a Ph.D. thesis. During the first year, candidates must pass qualifying examinations of high standard in theoretical chemistry before they are further considered for the research degree. All University fees will be paid, and the yearly stipend will be $3,600.

Applicants should write to Mr. James Malone, Department of Chemistry, John Harrison Laboratory of Chemistry, University of Pennsylvania, Philadelphia 4, Pa., before April 1, 1961.

MANSFIELD HOSPITAL MANAGEMENT COMMITTEE

Whole-time Biochemist (non-resident) required for hospital biochemical work in the Mansfield Area Pathology Service. The salary is that of the N.H.S. Basic Grade with a maximum of £1,035 per annum, the commencing salary being dependent upon qualifications and experience.

Applications to Hospital Secretary, King's Mill Hospital, Sutton-in-Ashfield, Notts.

SK&F

offer an unusual opportunity in their

PHARMACOLOGY DEPARTMENT

This post is newly created on a senior level and calls for considerable intellectual ability and initiative.

The minimum qualifications required are a good Honours Degree in Physiology, Pharmacology, or a related subject, and several years research experience, either in an academic institution or in industry.

The duties and responsibilities of the post will be based on the interests and previous experience of the successful applicant. Although he will be expected to participate in the normal research activities of the Department, it is also anticipated that he will spend a considerable part of his working time on projects of his own choosing. These will preferably be orientated towards an elucidation of the biochemical and/or physiological mechanisms underlying the actions of new synthetic drugs, or a study of selected body processes, a better understanding of which might lead to new lines of therapeutic advance.

A substantial starting salary with annual merit reviews and congenial working conditions in new and well-equipped laboratories will be provided. Other Company benefits include a non-contributory Pension and Life Assurance Scheme and full payment of removal expenses. Under certain circumstances a married man may be eligible for rented unfurnished accommodation.

Letters of application, giving fullest possible details considered relevant should be addressed to:

SK&F

The Employment Officer
SMITH KLINE & FRENCH LABORATORIES LTD.
Mundells, Welwyn Garden City, Herts.
Quoting Reference No. L.1448.

MIDDLESEX COUNTY COUNCIL EDUCATION COMMITTEE

ACTON TECHNICAL COLLEGE HIGH STREET, ACTON, W.3

Principal: W. F. Giddings, B.Sc.(Eng.)

Applications are invited for the following post, duties to commence September 1, 1961:

Assistant Grade B, to teach Zoology and Botany to classes for General Certificate of Education, Advanced Level, and the Ordinary Endorsed Certificate in Biology. The successful candidate would be expected to help with field work. Applicants should be University graduates.

Salary within the range £828 to £1,486 per annum.

Forms of application and further particulars may be obtained from the Principal (foolscap s.a.e.) to whom the completed forms should be returned within fourteen days of the appearance of this advertisement.

C. E. GURR, M.Sc., Ph.D.,
Chief Education Officer.

UNIVERSITY OF KHARTOUM

Applications are invited for the Chair of Agriculture, the Chair of Geography, and the Chair of Physics. Salary scale: Professor, £S.2,760 per annum. Cost of living allowance approximately £S.180 per annum at present. Outfit allowance £S.50. Family allowances: wife, £S.60 per annum; first child, £S.90 per annum; second and third child, £S.30 per annum each. (£S.1 = £1 0s. 6d. sterling). Passages for appointee and family on appointment, termination and annual leave. There is a superannuation scheme and arrangements can be made to maintain F.S.S.U. policies. Appointment on contract for five years with possibility of renewal. Unfurnished accommodation provided at rent (excluding rates) up to 7½ per cent of salary.

Applications (ten copies), detailing qualifications and experience and naming three referees by April 15, 1961, to Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

BIRKBECK COLLEGE
(UNIVERSITY OF LONDON)

—A—Senior Research Assistant of postdoctoral standard, qualified in inorganic chemistry, is required for two years to take part in an investigation of the crystal chemistry of oxides and hydroxides of the transition metals. There will be opportunities for acquiring experience with X-ray and electron diffraction techniques. The salary will be about £1,100 per annum.

Further particulars should be obtained from the Secretary, Birkbeck College, Malet Street, W.C.1. Closing date April 5.

UNIVERSITY OF KHARTOUM

Applications are invited for a Readership or Senior Lectureship or Lectureship in Zoology, and for a Senior Lectureship or Lectureship in Mathematics. Salary scales: Reader, £S.2,175 per annum; Senior Lecturer, £S.2,052 by £S.75 to £S.2,127 per annum; Lecturer, £S.1,077 by £S.75 to £S.1,977 per annum. Entry point according to qualifications and experience. Cost of living allowance approximately £S.180 per annum at present. Outfit allowance £S.50. Family allowances: wife, £S.60 per annum; first child, £S.90 per annum; second and third child, £S.30 per annum each. (£S.1 = £1 0s. 6d. sterling). Passages for appointee and family on appointment, termination and annual leave. There is a superannuation scheme, and arrangements can be made to maintain F.S.S.U. policies. Appointment on contract for five years with possibility of renewal. Unfurnished accommodation provided at rent (excluding rates) up to 7½ per cent of salary.

Applications (ten copies) detailing qualifications and experience and naming three referees by April 15, 1961, to Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

NOTTINGHAM AND DISTRICT TECHNICAL COLLEGE

BURTON STREET, NOTTINGHAM

Principal: D. A. R. Clark, M.Sc.(Tech.), M.I.Mech.E.

Applications are invited for the following posts: Lecturer in Physical Chemistry; Lecturer in Inorganic Chemistry. Appointment to take effect on May 1, 1961, or as soon as possible thereafter. The work includes the teaching of the above subjects to the standard of Grad.R.I.C. and B.Sc. Research and/or industrial experience would be an advantage. Salary in accordance with the Burnham Technical Scale: £1,370 by £35 to £1,550 per annum. A salary above the minimum will be paid in approved cases. Research encouraged. Facilities and equipment available.

Further particulars and form of application may be obtained from the Principal to whom completed forms should be returned not later than March 31, 1961.

ASSISTANT EXPERIMENTAL OFFICER required at the National Vegetable Research Station, Wellesbourne, Warwick, for the Plant Breeding Section to assist in breeding programmes and to do cytological checks on breeding material. Qualifications: Degree (science or horticulture) or equivalent. Salary in scale £578 per annum at age 21 to £983. Contributory superannuation scheme. —Applications, with names of two referees, to Secretary, National Vegetable Research Station, Wellesbourne, Warwick, by April 1, 1961.

MONMOUTHSHIRE EDUCATION COMMITTEE

THE TECHNICAL COLLEGE OF MONMOUTHSHIRE

Principal: T. V. Starkey, B.Sc., Ph.D., F.Inst.P.

Applications are invited for appointments from September 1, 1961, as follows:

S(1) Assistant to teach General Science and particularly Biology and Human Biology. Candidates must be qualified or experienced Teachers preferably holding Graduate qualifications.

S(2) Assistant to teach Mathematics with some Physics. Candidates must be qualified or experienced Teachers preferably with Graduate or equivalent qualifications.

S(3) Assistant to teach Physics preferably with some Metallurgy. Candidates should hold Graduate or equivalent qualifications. Industrial or teaching experience would be an added recommendation.

Salary for the above Posts will be in accordance with the Burnham Scale for Assistant Lecturers Grade "A." Forms of application and further particulars can be obtained from the undersigned, to whom completed forms should be returned not later than March 31, 1961.

T. M. MORGAN,
Director of Education.

County Hall,
Newport, Mon.

BRITISH EMPIRE CANCER CAMPAIGN

RADIATION RESEARCH

A graduate electrical or electronics engineer, age preferably 25 to 30, is required to collaborate in the development and experimental use of an electron linear accelerator, 3 cm. microwave spectroscopic and other experimental equipment which is being used to study the chemical and biological effects of microsecond pulses of radiation. Salary in accordance with qualifications and experience.

Apply in writing to the Director, Research Unit in Radiobiology, Mount Vernon Hospital, Northwood, Middlesex.

TECHNICIAN (FEMALE) REQUIRED FOR new expanding Physics Laboratory. Salary at minimum age 21: £570 rising to £710 per annum. Qualifications G.C.E. "A" level in physics and mathematics or similar. Work chiefly concerned with diagnosis and treatment using radioactive isotopes. Alternatively, Technician-in-Training. Salary at age 16, £215 rising to £440 per annum, with prospects of promotion to Technician on obtaining requisite qualifications.—Further particulars from Hospital Secretary, Dudley Road, Hospital, Birmingham 18.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

SCIENTIFIC GLASSBLOWER

The Organization's **Division of Chemical Physics, Chemical Research Laboratories, Melbourne,** invites applications for the position of Scientific Glassblower to assist the research staff in the design, construction and maintenance of a variety of glass apparatus.

Applicants should possess experience in Scientific glass working including bench, hand-torch and glass-lathe work and additional experience with both hard and soft glasses, fused silica and glass-to-metal seals is essential. A knowledge of laboratory techniques, such as production and measurement of high-vacuum, is desirable.

Salary: Dependent on qualifications and experience within the ranges: £A.1,334 to £A.1,510 per annum, or £A.1,510 to £A.1,620 per annum.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Fares paid. Further particulars of conditions, etc., supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting Appointment No. 581/12) should be addressed by April 15, 1961.

Research Director

U.S. company with international activities and American research laboratories requires a Research Director for new, small, physical science laboratory outside London (near Henley). Director will maintain liaison with British and European science and act as technical advisor on company activities in Great Britain and Europe. Research experience required, and doctoral degree desirable.

Salary £3,500 to £5,000

depending upon qualifications.

Send relevant details to Box 957, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

Strictest confidence will be maintained.

NEW RESEARCH LABORATORY

LONDON TRANSPORT is expanding its scientific activities and SCIENTISTS are required for the new research laboratory at Chiswick.

Candidates should possess a first- or second-class Honours degree in Chemistry or Metallurgy, or an equivalent qualification, preferably with previous experience. Consideration will also be given to candidates who will have completed their POST-GRADUATE studies or who will be GRADUATING this summer.

Applications are invited for the following vacancies:

POST A: FUELS AND LUBRICANTS SECTION. For duties concerned with the testing and evaluation of liquid fuels, lubricating oils, greases and other end products of the petroleum industry; service tests are also carried out in collaboration with the Engineering Departments.

POST B: PAINTS AND PROTECTIVE PROCESSES SECTION. For analytical work involving paints, paint materials and allied products.

POST C: GENERAL CHEMISTRY SECTION. For analytical work and investigation of problems, both of a very varied nature.

POST D: METALS SECTION. For duties concerned with metallography and physical testing. Experience in radiographic examination of metals would be an advantage.

Salaries within the range of:
£1,140 per annum to £1,320 per annum
or
£750 per annum to £1,140 per annum
according to age, qualifications and experience.

VALUABLE FREE TRAVEL;
FIVE-DAY WEEK;
CONTRIBUTORY SUPERANNUATION.

Applications to Staff and Welfare Officer, LONDON TRANSPORT, 55 Broadway, S.W.1, stating post applied for and quoting reference No. 133/2.

UNIVERSITY OF MANCHESTER

Applications are invited for the post of Assistant Lecturer in Biophysics in the Faculty of Medicine. The post is newly established and applicants should have been trained in electron microscopic techniques. Duties to commence June 1, 1961, or as soon as possible thereafter. Salary on a scale £800 to £950 per annum with membership of F.S.S.U. and Children's Allowance Scheme.

Applications should be sent not later than March 25, 1961, to the Registrar, the University, Manchester 13, from whom further particulars and forms of application may be obtained.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3

DEPARTMENT OF BOTANY AND ZOOLOGY

The Governing Body invite applications for the post of Zoology Assistant (Grade B). Candidates should possess good academic qualifications. Duties to commence September 1, 1961. Salary scale: Assistant (Grade B), £700 by £27 10s. to £1,150, plus additions for training and graduate status. There is, in addition, a London allowance of £38 or £51 according to age.

Particulars and forms of application from the Clerk to the Governors, to whom applications should be submitted not later than April 10, 1961.

DALHOUSIE UNIVERSITY

HALIFAX, NOVA SCOTIA, CANADA

As part of an expansion programme applications are invited for the following positions:

Assistant Professor in Microanatomy to teach medical and science students and conduct research in embryology. Preference will be given to candidates with a science degree in zoology or medical qualification.

Assistant Professor in Gross Anatomy primarily to teach gross anatomy, with opportunities to participate in research and in other responsibilities of the department. Modern facilities for research available. The salary for an Assistant Professor with medical qualifications will be not less than $8,500, depending upon qualification.

Inquiries for both appointments should be addressed to Professor R. L. de C. H. Saunders at the above address.

MAY & BAKER LTD DAGENHAM ESSEX require in their Publicity Division a young lady of good scientific education to assist in the interesting work of editing publications on chemical, pharmaceutical, horticultural, photographic and other subjects. A good knowledge of written English is necessary, and previous experience would be useful, although not essential.—Write, giving full particulars of qualifications and experience, to the Personnel Officer, quoting Reference No. N/77/60.

UNIVERSITY COLLEGE OF THE WEST INDIES

Applications are invited for: (i) Senior Lectureship or Lectureship in Theoretical Physics; (ii) Lectureship or Assistant Lectureship in Zoology. Salary scales: Senior Lecturer, £1,500 by £75 to £2,425 per annum; Lecturer, £1,050 by £50 to £1,400 by £75 to £1,850 per annum; Assistant Lecturer, £800 by £50 to £950 per annum, all plus local allowance of £250 per annum (pensionable). Entry point determined by qualifications and experience. Child allowance. F.S.S.U. Unfurnished accommodation at rental of 10 per cent of basic salary. Up to five full passages on appointment, normal termination and triennial study leave.

Detailed applications (six copies), naming three referees, by April 17, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

BUILDING RESEARCH STATION (D.S.I.R.), Garston, near Watford, Herts, requires Physicists as Scientific/Senior Scientific Officers to carry out research into physics of buildings. Research falls into categories of heat and radiation transfer; air movement and convection; elastic vibration in solid structures, transmission of sound in the atmosphere; climatology and meteorology in relation to buildings; physics and psychophysics of lighting of buildings. Design of buildings has hitherto been based on traditional concepts and scientific study of physical environment criteria promises to be an extremely rewarding new field of research. Qualifications: first- or second-class honours degree in physics. For Senior Scientific Officer at least three years' postgraduate experience required and minimum age 26. Salary ranges: (Men) Scientific Officer, £717 to £1,186; Senior Scientific Officer, £1,302 to £1,604.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.89/1A. Closing date April 24, 1961.

ROYAL COLLEGE
NAIROBI

Applications are invited for (1) Senior Lectureship in Physics. (2) Senior Lectureship in Electrical Engineering from graduates with corporate membership of Institution of Electrical Engineers. (3) Lectureship in Botany. (4) Lectureship or Assistant Lectureship in Chemistry. Qualifications in Physical and/or Inorganic Chemistry preferred. (5) Lectureship in Geology. Qualifications and/or experience in Palaeontology, Stratigraphy, or Structural Physical Geology preferred. Salary scales: Senior Lecturer, £1,950 by £75 to £2,475 per annum; Lecturer, £1,350 by £51 to £1,707 by £72 to £1,851 by £75 to £2,151 per annum; Assistant Lecturer, £1,100 by £50 to £1,250 per annum. Entry point determined by qualifications and experience. F.S.S.U. Child allowance £50 per annum per child (maximum £150 per annum). Passages for appointee and family (up to four adult passages) on appointment, termination and leave (once every two years). Rent according to quarters provided £60 to £114 per annum.

Detailed applications (six copies), naming three referees, by April 25, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

NEW ZEALAND
AGRICULTURE DEPARTMENT

Applications are invited for the undermentioned vacancies:

No. 457: Veterinary Research Officer (Pathologist), Wallaceville Agriculture Department, New Zealand. Commencing salary: Up to £1,700 (automatic adjustment to £1,800 on April 1, 1961). Further advancement is on merit and an outstanding officer may proceed to £2,300. Qualifications desired: Degree in veterinary science with posteraduate training and experience in histopathology. Duties: Application of pathology to the diagnosis of diseases of farm animals and associated research.

No. 458: Veterinary Research Officer (Microbiologist), Wallaceville, Agriculture Department, New Zealand. Commencing salary: Up to £1,700 (automatic adjustment to £1,800 on April 1, 1961). Further advancement is on merit and an outstanding officer may proceed to £2,300. Qualifications desired: Degree in veterinary science with posteraduate training and experience in microbiology. Duties: Research into infectious diseases of farm animals and their control.

Passages: Steamer fares of up to £165 each for the appointee and his wife, and pro rata for dependent children will be paid. Incidental expenses: Up to £35 for a single person and £100 for a married man can be claimed to cover the cost of taking personal effects to New Zealand.

Inquiries, quoting reference number B.13/2/1, should be addressed to the High Commissioner for New Zealand, 415 Strand, London, W.C.2, who will furnish further details and application forms. Completed applications to be lodged with this office not later than April 15, 1961.

MEMORIAL UNIVERSITY OF NEWFOUNDLAND
ST. JOHN'S, NEWFOUNDLAND, CANADA

Applications are invited for the position Assistant Professor of Biology with specialization in animal physiology, embryology and histology. Candidates with background and experience in marine biology will receive preference. Ph.D. or equivalent essential. Duties beginning September 1961, to include teaching and research. The starting salary will be based on qualifications and experience.

Applications, accompanied by complete curriculum vitae and the names of three references, should be addressed to the Head, Department of Biology, Memorial University of Newfoundland.

BUILDING RESEARCH STATION (D.S.I.R.), Garston, near Watford, Herts., requires civil or structural engineers as Scientific/Senior Scientific Officers for research on concrete construction for nuclear power stations, design of multi-story buildings, light-weight reinforced concrete, ultimate strength design, earth retaining structures, earth pressures on tunnels, and other projects in structural and civil engineering. Work involves laboratory studies up to model scale and field measurement on actual structures, all with first-class facilities. Qualifications: first- or second-class honours degree in civil or structural engineering. For Senior Scientific Officer at least three years postgraduate experience and minimum age 26. Salary ranges (men): Scientific Officer, £717 to £1,186; Senior Scientific Officer, £1,302 to £1,604.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting E.340/OA. Closing date April 4, 1961.

COLLEGE OF ADVANCED TECHNOLOGY, BIRMINGHAM

Applications are invited for the following posts:

Department of Mathematics

PRINCIPAL LECTURER	in STATISTICS
SENIOR LECTURER	in MATHEMATICS
LECTURER	in MATHEMATICS or STATISTICS

Department of Chemistry

READERS	in INDUSTRIAL CHEMISTRY in CHEMICAL ENGINEERING
PRINCIPAL LECTURER	in GAS and CHEMICAL ENGINEERING
SENIOR LECTURER	in INORGANIC AND ANALYTICAL CHEMISTRY or RADIOCHEMISTRY
LECTURER	in PHYSICAL CHEMISTRY with special reference to INFRA-RED SPECTROSCOPY

Department of Physics

SENIOR LECTURER	in PHYSICS (with experience in Electron Microscopy)
LECTURER	in PHYSICS
LECTURER	in OPHTHALMIC OPTICS

Salary Scales:

Readers	£1,800 to £2,100
Principal Lecturers	£1,750 to £1,900
Senior Lecturers	£1,550 to £1,750
Lecturers	£1,370 to £1,550

Further particulars and forms of application from the Bursar, College of Advanced Technology, Gosta Green, Birmingham, 4. Applications to be received within fourteen days of this advertisement. Please quote 361D.

K. R. PILLING, Clerk to the Governors.

SENIOR PHYSICIST

required by

British-American Tobacco Company Limited

for its Research and Development Establishment (Southampton). He should be experienced and well qualified in classical physics but have a special interest in one or more of the following fields: mathematical physics, diffusion and drying, electronic and general instrument design, process control, statistical quality control, or spectroscopy. Although there will be considerable scope for basic research, the successful applicant will be interested in the application of research work to commercial problems. The Establishment is situated in a primarily non-industrial area with easy access to the New Forest and the Solent.

Written applications to Personnel Dept. (No. 5),

British-American Tobacco Co. Ltd.,
Westminster House, 7 Millbank, London, S.W.1.

INSTITUTE OF CHILD HEALTH
UNIVERSITY OF LONDON

Laboratory Technician required for the Neonatal Unit at the Hammersmith Hospital, Ducane Road, W.12. Biochemical experience an advantage. A.I.M.L.T. or equivalent preferred. Salary, Senior Technician II, Whitley Scales.

Apply to the Secretary, Institute of Child Health, The Hospital for Sick Children, Great Ormond Street, W.C.1, giving age, experience, and qualifications.

UNIVERSITY OF OTTAWA
DEPARTMENT OF CHEMISTRY

Applications are invited for an Associate Professorship in the field of organic chemistry. Candidates should be active research workers with several years' experience of University lecturing.

Applications, including a curriculum vitae, a list of published papers, and the names of two referees, should be sent as soon as possible to Professor K. J. Laidler, Department of Chemistry, University of Ottawa, Ottawa 2, Canada.

THE PATENT OFFICE

offers an interesting, well paid job with good prospects to suitably qualified men and women in congenial working conditions.

interest You will be dealing with inventions from the whole world in your chosen subject. By its very nature the work will inevitably maintain your knowledge of science and technology completely up to date and will give you inside knowledge of new manufactures well ahead of the public at large.

salary The training salary for the first two years is £793 and £824. On satisfactory completion the scale is £941–£1,719 by regular increments, but there is a jump in the scale to £1,324 five years after entry, or only four or even three in cases of special merit. Approved postgraduate experience fetches a higher starting salary. One promotion only, of which prospects are excellent, raises your maximum to £2,715. Reasonable proportion of still higher posts up to £3,865 all filled exclusively by promotions from entry grade.

qualifications Age 21–36 and first- or second-class honours degree in physics, chemistry, engineering or mathematics, or an equivalent such as A.R.I.C., A.Inst.P., or corporate membership of I.C.E., I.Mech.E., or I.E.E., or first- or second-class honours Diploma of Technology.

conditions Location, London, five-day week. Annual leave 4½ rising to 6 weeks. Posts are permanent and pensionable (non-contributory).

Write or telephone for further information, or for a visit to the Patent Office to see the work, entirely without obligation. **The Superintending Examiner (B Staff), The Patent Office, 25 Southampton Buildings, London, W.C.2. Telephone** HOLBORN 8721. **Ext.** 324.

ABSTRACTOR

An abstractor is wanted for the comprehensive technical library maintained by I.C.I. Nobel Division at Stevenston, Ayrshire. This library is part of the Division's large Research and Development Department and it provides an essential service.

The abstractor's work will be with scientific journals written in English, and the subjects of special interest will be Explosives Technology, Cellulose Chemistry, Organo Metallics, and General Chemistry.

Qualifications for the post imply a scientific background, and the applicant should have attained a B.Sc. at ordinary level or its equivalent in Chemistry and Physics.

The work is interesting and the successful candidate would assist with the filing of information in a Central Technical Index. Previous library and indexing experience would, therefore, be desirable, but it is not essential.

Conditions of employment are attractive. The Company operates a five-day week, a contributory Staff Pension Fund, and a Profit-sharing Scheme.

Applications, giving age, qualifications, and previous experience, should be sent to the

Staff Manager,
Imperial Chemical Industries Limited,
Nobel Division,
460 Sauchiehall Street,
Glasgow, C.2.

SHELL

"SHELL" RESEARCH LTD.

require

ANALYTICAL CHEMISTS

in their Analytical Division at

WOODSTOCK AGRICULTURAL RESEARCH CENTRE

near Sittingbourne, Kent

Applicants, aged under 30, should possess B.Sc., A.R.I.C., or Grad.R.I.C. qualifications. Experience in one or more of the following fields is desirable: Organic Micro-analysis; chemical spectroscopy; general organic analysis; examination of agricultural technical products and formulations; soil, grass and fertiliser analysis; determination of toxicant residues in crops or animal products.

Five-day week, staff restaurant, sports and social facilities, attractive pension scheme.

Please write, giving full details of age, experience and qualifications, to:

Personnel/Recruitment/A.C./2,
"Shell" Research Limited,
St. Helen's Court,
London, E.C.3.

NIGERIAN COLLEGE OF ARTS, SCIENCE AND TECHNOLOGY

ZARIA BRANCH

Applications are invited for the post of Lecturer in Zoology. Candidates should have a good honours degree, teaching experience up to degree level, and research experience. Appointment will be for two tours in the first instance. Contract salary scale £792 to £1,760. Entry point according to qualifications and experience. Gratuity of £25 to £37 10s. for each completed three months' residential service. Addition of £180 to £300 per annum for overseas appointees. Partly furnished quarters at one-twelfth basic salary rental. Free passages, including wife. Children's U.K. maintenance grant up to £150 per annum and passage assistance. Tours 10 to 18 months, but leave normally taken in long vacation.

Further information obtainable from the Council for Overseas College, 12 Lincoln's Inn Fields, W.C.2, to whom applications (eight copies), giving age, qualifications, experience and the names of three referees, should be submitted before April 7, 1961.

GLASSBLOWER

CHEMISTRY DEPARTMENT, QUEEN'S UNIVERSITY, KINGSTON, ONTARIO, CANADA

A Glassblower is required for the Chemistry Department. Salary according to qualifications.

Please write, including two recommendations, to Dr. J. K. N. Jones.

UNIVERSITY OF BRITISH COLUMBIA

PHYSICS

Applications are invited for appointments to the teaching and research staff as well as for postgraduate fellowships and scholarships for the Session commencing in September, 1961. There are specific vacancies at the Assistant Professor level in Optical Spectroscopy, Meteorology and Low Energy Theoretical Nuclear Physics. Applications in other fields of physics will also be considered.

Further information and a copy of an illustrated brochure describing the activities and facilities of the Department may be obtained by writing to G. M. Shrum, Head, Department of Physics, University of British Columbia, Vancouver 8, B.C. Professor Shrum expects to be in London from March 16 to 25 and will be pleased to arrange personal interviews. Inquiries should be directed to B.C. House, 1 Lower Regent Street, London, S.W.1.

NEW ZEALAND EDUCATION DEPARTMENT

Applications are invited for the following positions at the New Zealand School of Pharmacy:

SENIOR TUTOR OR TUTOR IN PHARMACEUTICS

Applicants should possess a degree or registrable qualification in pharmacy and have had teaching experience. A post-graduate qualification and/or research experience would be an additional advantage.

The appointee will be in charge of all the teaching in pharmaceutics and will be particularly responsible for the teaching of pharmaceutical microbiology.

TUTOR OR ASSISTANT TUTOR IN PHARMACOGNOSY

Applicants should possess a degree or registrable qualification in pharmacy. A postgraduate qualification, teaching or research experience would be an additional advantage. The appointee will be responsible for all the teaching in Pharmacognosy and should also be prepared to assist with the teaching of pharmaceutics.

SENIOR TUTOR OR TUTOR IN PHARMACEUTICAL CHEMISTRY

Applicants should possess a degree or registrable qualification in pharmacy and should preferably have had teaching experience. The ability to teach pharmacognosy would be an additional advantage.

Salary (operative from April 1, 1961):
Senior Tutor in the range £1,515 to £1,705.
Tutor in the range £1,260 to £1,515.
Assistant Tutor in the range £910 to £1,260.

The scales apply to both male and female staff and the commencing salary will depend on qualifications and experience.

Passages: Steamer fares of up to £165 each for the appointee and his wife, and pro rata for dependent children will be paid.

Incidental expenses: Up to £35 for a single person and £100 for a married man can be claimed to cover the cost of taking personal effects to New Zealand.

Inquiries quoting reference number B11/8/9 should be addressed to the High Commissioner for New Zealand, 415 Strand, London, W.C.2, who will supply further details and application forms.

Completed applications to be lodged with his office not later than April 10, 1961.

UNIVERSITY OF READING

Applications are invited for a senior appointment as Research Physicist in the Department of Physics in the field of vacuum spectroscopy. The work will involve measurements of absorption spectra of gases and vapours. Experience in vacuum technique is essential but the spectroscopy should present no serious difficulty to a candidate who has a good degree. The salary is according to qualifications and experience and has been estimated on the basis that the person appointed will have recently taken his Ph.D. degree. A higher salary may be paid to a person who has had some further experience in research. A small amount of teaching work in the Department may be included if desired.

Applications should be sent to Professor R. W. Ditchburn, J. J. Thomson Physical Laboratory, Whiteknights Park, Reading, not later than May 1, 1961.

MEMORIAL UNIVERSITY OF NEWFOUNDLAND

ST. JOHN'S, NEWFOUNDLAND, CANADA

Applications are invited for the position Assistant Professor of Biology with specialization in invertebrate zoology. Candidates with background and experience in marine biology will receive preference. Ph.D. or equivalent essential. Duties beginning September, 1961, to include teaching and research.

Applications, accompanied by complete curriculum vitae and the names of three references, should be addressed to the Head, Department of Biology, Memorial University of Newfoundland.

COLUMBIA UNIVERSITY

RESEARCH APPOINTMENTS IN X-RAY CRYSTALLOGRAPHY

Applications are invited for two post-doctoral appointments in X-ray Crystallography in the Department of Biochemistry. The principal research problems under investigation are the crystal structure analyses of the protein hormone insulin and the peptide hormone oxytocin. One of these appointments is open to candidates with special interests in computing methods and in the computing problems associated with the determination of the structure of large molecules. Some previous experience in computer programming would be an advantage. The appointee will work initially with a member of the research group experienced in this field. Computational facilities, IBM 650, 709 and 7090 are available. Candidates for both appointments should have a doctoral degree, or its equivalent in experience, and have undertaken research in single crystal structure determination. Opportunities will be available to candidates with an interest in teaching X-ray crystallography. The salary offered will be determined by qualifications and experience. The appointments are for a minimum period of two years.

Applications and requests for further information should be sent to Dr. Barbara W. Low, Department of Biochemistry, College of Physicians and Surgeons, 630 West 168th Street, New York 32, N.Y.

NORTHAMPTON COLLEGE

ST. JOHN STREET, LONDON, W.1

HEAD OF MATHEMATICS DEPARTMENT

The Governing Body invites applications for the appointment of Head of the Department of Mathematics as a successor to Mr. A. Geary, M.A., M.Sc., who retires at the end of the present session. The work of the Department, within the College of Advanced Technology, is concerned exclusively with B.Sc.(Eng.), Diploma-in-Technology and postgraduate studies. It is entirely responsible for a Diploma-in-Technology in Applied Mathematics and for a growing Laboratory which includes analogue and digital electronic computers. Salary scale: Grade VI under the current Burnham Technical Award, viz.: £2,250 per annum by increments of £50 to £2,500 per annum (plus London allowance £38 to £51 per annum).

Further particulars and application form from the Secretary of the College. Applications must be submitted not later than March 31, 1961.

J. S. TAIT, Ph.D., B.Sc.(Eng.), A.R.I.C., M.I.E.E., M.I.Mech.E., Principal.

DAIRY RESEARCH INSTITUTE

NEW ZEALAND

Applications are invited for the following research staff. Chemist for research on the chemistry of dairy products. Biochemist-Bacteriologist for work mainly in connection with the manufacture and ripening of cheese. Salaries are in the ranges £900 to £1,210, £1,250 to £1,700, £1,750 to £2,000. Travel and other removal expenses are allowed within certain limits.

Further particulars may be obtained in Britain from Mr. P. S. Robertson, c/o N.I.R.D., Shinfield, near Reading.

D.S.I.R., ROAD RESEARCH LABORATORY, Harmondsworth, Middlesex, requires Senior Scientific/Scientific Officers and Experimental Assistant Experimental Officers (Civil Engineers, Physicists and Mathematicians) for work on the following: (1) Assessment, measurement and analysis of strains, stresses and deformations imposed on bridge and flyover structures of various types and on elevated roads by traffic loading, impact, settlement and climatic variation. (2) Effects of vibration and fatigues. (3) Study of design methods of complex bridge structures. (4) Design of bearings and hinges, parapets, joints, etc. (5) Maintenance problems. (6) Strength, elastic and rheological properties of bridge-making materials. Electronic and other techniques will be applied and a computer available where necessary. Qualifications. Scientific Officer Grades: first- or second-class honours degree or equivalent in appropriate subject. Senior Scientific Officer: at least three years appropriate postgraduate research experience required. Assistant Experimental Officer (age 22 or over): Experimental Officer (age 26 or over). Pass degree or equivalent in appropriate subject. Salary: Scientific Officer, £773 to £1,267; Senior Scientific Officer, £1,392 to £1,714. Normal prospects of promotion in mid-thirties to Principal Scientific Officer (£1,776 to £2,478). Assistant Experimental Officer, £680 (age 22) to £1,023; Experimental Officer, £1,132 to £1,386.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting E.77/1A.

LEYBOLD-ELLIOTT LIMITED

require a SENIOR PHYSICIST to lead a research and development team on investigations into leak detection, gas analysis and ultra-high vacuum techniques.

The appointment offers ample scope and opportunity for initiative and originality over a wide field of vacuum physics or engineering with application to Satellite Studies, Ion Motors, Distillation and Impregnation.

Candidates should have a good degree in Physics with preferably several years' post-graduate experience.

Commencing salary for this post would be in accordance with age and experience.

Write, giving full details to:

The General Manager (Ref. 343)
LEYBOLD-ELLIOTT LIMITED,
Manor Way, Borehamwood, Herts.

NOTTINGHAM AND DISTRICT TECHNICAL COLLEGE

BURTON STREET, NOTTINGHAM

Principal: D. A. R. Clark, M.Sc.(Tech.), M.I.Mech.E.

Applications are invited for the following full-time posts of Research Associate:

Physics. Candidates should possess a good degree in physics or grouped subjects, including physics. The research will be on the physical properties of substances in the powdered state in connection with a research contract placed with the College by the United Kingdom Atomic Energy Authority. Much of the work would be suitable for a higher degree.

Applied Chemistry. Applicants should possess a degree or equivalent qualifications, with main interest in organic or physical chemistry. Research topics will be concerned with problems on the dyeing and finishing of textiles.

Mechanical Engineering. The person appointed will be expected to undertake research in one of the following fields: Vibration of Machine Tools; Vibration in Vehicles; Critical speeds and damping; Model analysis in production processes; Heat Transfer, Fatigue, or Metal Cutting. The post offers considerable scope and encouragement will be given to obtain higher qualifications.

The Research Associates will be required to assist generally with the research work of the Departments and in particular, to co-ordinate the work of part-time researchers. The posts are tenable for three years, renewable annually. Salary for the above posts: £750 by £50 to £850 per annum.

Application forms and further particulars may be obtained from the Principal, to whom they should be returned not later than March 24, 1961.

ZOOLOGIST FOR SQUIRREL RESEARCH. A pensionable post in Forestry Commission for a male or female Scientific Officer in a field research team working in the Guildford/Farnham area on squirrels and other mammalian forest pests, with special reference to ecology and relationship of red and grey squirrels, population studies, and development of new methods of control. Age: at least 21 and normally under 29 on December 31, 1961. Qualifications: first- or second-class honours degree in zoology and preferably some research experience. Knowledge or experience of forestry, ability to drive a car, aptitude for designing field equipment, and acquaintance with rural life and pursuits, are advantages. National salary on scale £738 to £1,222 according to experience, etc. Promotion prospects.—Write Civil Service Commission, 17 North Audley Street, London, W.1, for application form quoting **S/52/61/Z.** Early application advised.

LABORATORY TECHNICIAN REQUIRED for Biology at L.C.C. Furzedown College, Welham Road, S.W.17. (Women's college of 330 students training as teachers.) Some experience necessary. £420 at 21 to £580. Holders of recognized qualifications £500 at 21 to £660.—Forms, returnable within 14 days, from Secretary, quoting (Estab. 7/N/607/3).

MINERALOGIST
or
INORGANIC CHEMIST

required by the National Coal Board's Coal Survey Laboratory at Nottingham to study, as a member of a small team the mineral constituents of coal seams and associated strata by analytical (including spectroscopic) techniques and other means. Applicants should possess a good honours degree or equivalent qualification. The appointment is superannuable and salary will be according to age, experience and qualifications within £710 to £1,075.

Write for application form to Staff Department (X2181D), N.C.B., Hobart House, London, S.W.1, which should be returned before March 28, 1961.

QUEENSLAND INSTITUTE OF MEDICAL RESEARCH
BRISBANE, AUSTRALIA

Applications are invited for the position of Director of the above Institute. The duties are (1) to direct research work and control research staff of the Institute, (2) to continue to develop the Institute on a comprehensive research basis, and (3) to plan the permanent housing of Institute. To date, research has been almost entirely in the field of communicable disease. The salary is £A.4,583 per annum. Tenure is for seven years, with eligibility for reappointment. Technical and lay staff, other than term appointees, such as the Director, are subject to the Public Service Acts, and administration generally follows Public Service practice. Appointee will be required to commence duty as early as possible after August 1, 1961.

Applications close, on April 30, 1961, with Agent-General for Queensland, 409 and 410 Strand, London, W.C.2, from whom intending applicants should obtain application forms and further information.

UNIVERSITY OF LIVERPOOL

Applications are invited for Research Fellowships in Experimental Physics. Candidates should be of Ph.D. standard, with special aptitude for research in high or low energy nuclear physics. The Fellowships are tenable for not more than three years, at an initial emolument within the range £600 to £800 per annum, with F.S.S.U. benefits.

Applications, three copies, stating age, details of qualifications and experience, publications, research work in progress and completed, together with the names of two referees, should be received not later than May 1, 1961, by the Registrar, from whom further particulars may be obtained. (Candidates overseas who find it more convenient to do so may send one copy only by airmail). Quoting reference CV/N.

UNIVERSITY OF READING

A Lecturer in Biometry is required in the Faculty of Agriculture, to conduct teaching, research and consulting work. Salary within the scales: £1,050 to £1,475 or £1,475 to £1,850, depending on qualifications and experience.

Further particulars may be obtained from the Registrar (Room 22, O.R.B.), the University, Reading, by whom applications should be received by April 15, 1961.

BUILDING RESEARCH STATION (D.S.I.R.), Garston, near Watford, Herts., requires two mathematicians or mathematical physicists, to make theoretical studies in fields of engineering, soil mechanics, physics, chemistry, building operations and economics. Current investigations include design of concrete shields for nuclear reactors, pore water pressure in earth dams, effects of noise from jet aircraft. There is also scope for application of modern statistical techniques to design and analysis of experiments. Successful candidates would be given opportunities to specialize in one or two fields and to work in close collaboration with laboratory teams. Publications are encouraged and where suitable, work could be submitted for higher degrees. Qualifications: first- or second-class honours degree in mathematics or physics. For Senior Scientific Officer at least three years postgraduate experience required and minimum age 26. Salary ranges: (men) Scientific Officer, £717 to £1,186. Senior Scientific Officer, £1,302 to £1,604.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.88/1A. Closing date April 4, 1961.

AUSTRALIA
UNIVERSITY OF NEW SOUTH WALES
ASSOCIATE PROFESSOR—SCHOOL OF TEXTILE TECHNOLOGY

The University invites applications for appointment to the position of Associate Professor of Textile Technology. Commencing salary will be not less than £A.3,179 per annum. Applicants must have high academic qualifications in science, engineering or textile technology. The successful applicant will participate in teaching and administration within the school and will be expected to make a substantial contribution to the expanding postgraduate activities of the school. The present Head of the School is Professor Malcolm Chaikin. Subject to the consent of the Council of the University, Associate Professors may engage in a limited amount of higher consultative work. Associate Professors are eligible for six months' study leave on full salary after three years of service, or twelve months after six years of service. The successful applicant will be eligible, subject to satisfactory medical examination, to join the superannuation scheme, which provides for a pension of up to £A.1,600 per annum. The University reserves the right to fill the position by invitation. With the approval of the University and its bankers, married men may be assisted by loans to purchase a home. First-class ship fares to Sydney of appointee and family will be paid.

Four copies of applications should be lodged, together with a snapshot and the names of three referees, with the Agent-General for New South Wales, 56 Strand, London, W.C.2, and a copy forwarded by airmail in an envelope marked "University Appointment" to the Bursar, University of New South Wales, Box 1, Post Office, Kensington, New South Wales, Australia, before April 30, 1961.

ANIMAL HEALTH TRUST
WELLCOME VETERINARY RESEARCH FELLOWSHIPS
1961

Applications are invited for appointments to Wellcome Fellowships for whole-time research in connection with veterinary science or medicine, from any person who on October 1, 1961 is under 36 years of age and holds the Membership Diploma of the Royal College of Veterinary Surgeons or a good degree in any faculty relevant to veterinary science or medicine in any university in the British Commonwealth and Empire. Applicants are expected to have done some postgraduate work and to provide evidence that they have been able to make arrangements for the satisfactory conduct of the proposed research which must be in the broad field of veterinary science. A Fellowship may be awarded at an annual value of £850 rising by annual increments of £50. The Fellowship is subject to income tax and carries benefits under the F.S.S.U.; it is tenable for one year in the first instance, and by annual reappointment for a further period of two years at the discretion of the Advisory Committee. Election will be made in June, to take effect as from October 1, 1961. Closing date for receipt of application is Friday May 12, 1961.

Forms of application are obtainable from: The Scientific Director, The Animal Health Trust, 14 Ashley Place, Westminster, London, S.W.1.

UNIVERSITY OF GLASGOW
LECTURESHIPS IN EXPERIMENTAL AND THEORETICAL PHYSICS

Applications are invited for Lectureships in Experimental and Theoretical Physics. Salary scale: Senior Lecturer, £1,750 to £2,275 per annum; Lecturer, £1,050 to £1,850 per annum. Grade of appointment and initial salary according to experience and qualifications. F.S.S.U. and family allowance benefits. Successful applicants will be expected to prosecute research preferably in Nuclear or Elementary Particle Physics in addition to teaching duties.

Applications (eight copies), including the names of two referees, should be lodged, not later than April 15, 1961, with the undersigned, from whom further particulars may be obtained.

ROBT. T. HUTCHESON,
Secretary of University Court

THE BRITISH DRUG HOUSES LTD. HAVE a vacancy in their Production Department for an Organic Chemist aged 25 to 30, with a B.Sc. or equivalent, to supervise some aspects of their steroid hormone manufacture. Knowledge of this branch of chemistry is desirable and some supervisory experience would be advantageous. Salary according to qualifications. The Company operates a superannuation fund with life assurance and a profit sharing scheme.—Applications, with full details, to Personnel Manager, Ref. HAC/BS, The British Drug Houses Ltd., Graham Street, London, N.1.

BEECHAM GROUP
RESEARCH SCIENTIST

An opportunity with excellent prospects is being created by expansion activity in nutritional research.

A seasoned graduate (first- or second-class honours) is sought with experience in one or more of the following fields:

Biochemistry
Food Chemistry
Nutrition

A postgraduate qualification is desirable but appropriate experience would be an equivalent asset.

The successful applicant would work in the Basic Research Unit at Brentford and be directly responsible to the Manager of the Unit. Prospects are excellent for the right man.

Applications, giving full details of age, qualifications and experience, and quoting reference RS121, should be addressed to the Personnel Controller, Beecham Group Limited, Beecham House, Great West Road, Brentford, Middlesex.

AMENDED ADVERTISEMENT
UNIVERSITY COLLEGE OF GHANA

Applications are invited for Lectureship in Agricultural Botany. The successful candidate, who preferably should have served in the Tropics, should possess an honours degree in pure science with experience in the field of agriculture, or alternatively an honours degree in agriculture, with specialization in plant pathology and/or plant physiology. Salary scale (under review): £G.1,000 by £G.50 to £G.1,350 (bar) by £G.75 to £G.1,800; £G.1,850 per annum, entry point according to qualifications and experience, F.S.S.U. Outfit, family and other allowances. Passages for appointee and family on appointment, leave, and normal termination. Part-furnished accommodation at a charge not exceeding 7.5 per cent of salary.

Detailed applications (six copies), naming three referees, as soon as possible to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

UNIVERSITY OF KHARTOUM

Applications are invited for Senior Lectureship or Lectureship in Agricultural Engineering. Salary scales: Senior Lectureship, £S.2,052 by £S.75 to £S.2,127 per annum; Lectureship, £S.1,077 by £S.75 to £S.1,977 per annum. Entry point according to qualifications and experience. Cost of living allowance approximately £S.180 per annum at present. Outfit allowance £S.50. Family allowances: wife, £S.60 per annum; first child, £S.90 per annum; second and third child, £S.30 per annum each (£S.1 = £1 0s. 6d. sterling). Passages are paid for appointee and family on appointment, termination and annual leave. There is a superannuation scheme and arrangements can be made to maintain F.S.S.U. policies. Appointment on contract for five years, with possibility of renewal. Unfurnished accommodation provided at a rent (excluding rates) up to 7½ per cent of salary.

Applications (ten copies) detailing qualifications and experience and naming three referees by April 15, 1961, to Registrar, University of Khartoum, c/o Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

BRITISH PETROLEUM COMPANY LIMITED has vacancies for Reservoir Engineers in its Exploration Research Laboratories at Sunbury-on-Thames. The work involves the analysis and prediction of oilfield performance, and the development of new techniques, including model studies and the application of computers to the analysis of numerical data. Opportunities for short visits abroad may arise from time to time. Applicants must have a good honours degree in physics, mathematics or engineering. Practical or research experience in oilfield technology would be an advantage. Salary according to age, qualifications and experience. Non-contributory Pension Fund, Housing Scheme, Luncheon Club. Removal expenses and settling-in allowance payable in certain cases.—Write, giving full details, quoting reference H.5443, to Box 6568, c/o Hanway House, Clark's Place, E.C.2.

UNIVERSITY COLLEGE OF RHODESIA AND NYASALAND

Applications are invited for post of Chief Laboratory Steward in Department of Geology, from persons with experience in a University Department of Geology or similar experience such as in a Department of Geological Survey or the Laboratories of a mining company. Salary scale: £1,100 by £50 to £1,500 per annum, entry point according to qualifications and experience. Superannuation and medical aid schemes. Passages to Salisbury for appointee, wife and dependent children with allowance for transport of effects. Unfurnished accommodation at rent of 15 per cent of salary.

Detailed applications (six copies), naming three referees, by April 10, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

UNIVERSITY OF ABERDEEN

Applications are invited for the following posts:

DEPARTMENT OF MATERIA MEDICA AND THERAPEUTICS

Lecturer in Therapeutics. Higher qualification in medicine required. Duties include clinical responsibility (with appropriate clinical status), teaching and research in general medical unit with interests in metabolic disease. Salary on scale: £1,100 to £2,350.

DEPARTMENT OF STATISTICS AND SOCIAL MEDICINE

Lecturer holding a Joint Appointment in the Departments of Statistics and Social Medicine. Salary on scale £1,050 to £1,850.

For either post, salary with placing according to qualifications and experience. F.S.S.U., child allowance and removal allowance.

Further particulars should be obtained from the Secretary, the University, Aberdeen, with whom applications (eight copies), should be lodged as follows: Therapeutics, not later than April 12, 1961. Statistics, etc., not later than March 31, 1961.

GRADUATE CHEMIST AND SENIOR TECHNICIAN

A New Zealand company engaged in chemical industry has positions available for suitable persons who have either graduated in Chemistry or who have had experience as a technician in an industrial chemical laboratory. Selected applicants would receive assistance in emigrating to New Zealand and would be bound to serve with the company for a minimum period of two years.

Bona fide inquiries should be sent in the first instance by airmail to the Works Director, Ivon Watkins Limited, P.O. Box 144, New Plymouth, New Zealand. Following receipt of such inquiries, which should include as much information as possible giving age, marital status, qualifications and experience and accompanied by *copies only* of testimonials, arrangements will be made for interview in the United Kingdom (preferably in May) when the Managing Director will be visiting England. Inquirers will be advised of time and place of interview.

Ivon Watkins Limited is a New Zealand company actively engaged in the development of chemical industry and offers unique opportunities to graduates and technicians with some experience in chemical industry.

UNIVERSITY OF LIVERPOOL

CHAIR OF VETERINARY ANATOMY

Applications are invited for the Chair of Veterinary Anatomy. Applicants should have special interest and experience within the fields of veterinary or comparative anatomy, histology or embryology. Possession of a veterinary qualification is desirable but not essential.

Further particulars may be obtained from the undersigned, by whom fourteen copies of applications (one in the case of overseas candidates), should be received not later than April 29, 1961. Quoting reference CV/N.

STANLEY DUMBELL,
Registrar.

GEOLOGISTS: DEPARTMENT OF Scientific and Industrial Research. At least four pensionable posts in Geological Survey for men and women aged 21 and under 30 (31 for permanent members of Experimental Officer Class) on July 1, 1961; extension for candidates with regular Forces service or Overseas Civil Service. Qualifications: normally first- or second-class honours degree in geology. National salary scale £738 to £1,222. Starting pay may be above minimum. Promotion prospects.—Write Civil Service Commission, 17 North Audley Street, London, W.1, for application form, quoting **S/168/61**. Closing date April 19, 1961.

UNIVERSITY OF EDINBURGH

DEPARTMENT OF ZOOLOGY

Applications are invited for the post of Assistant in the Department of Zoology. Salary scale: £800 by £50 to £950 per annum, with superannuation benefit and family allowance where applicable. Tenure is normally for three years, with two possible annual extensions. The Assistant will be required to help in the general teaching of the Department, and will have ample facilities for research.

Further particulars may be obtained from the undersigned, with whom applications (six copies), giving the names of two referees, should be lodged as soon as possible, and not later than April 15, 1961.

CHARLES H. STEWART,
Secretary to the University.

VACANCIES FOR GRADUATES IN ZOOLOGY

Assistant Inspectors of Fisheries (male) (3) required by Department of Lands, Dublin. Commencing salary up to £768, maximum salary £1,205. Maximum age limit: 40 years, with extensions. Essential: degree (or equivalent) which required an adequate course of study in zoology.

Application forms, etc., from Secretary, Civil Service Commission, 45 Upper O'Connell Street, Dublin, 1. Latest time for receiving completed application forms: 5 p.m. on April 7, 1961.

WELLCOME RESEARCH LABORATORIES

A vacancy for a science graduate exists in the Immunology Department. The work will be concerned with bacterial toxins and antitoxins and general immunological problems, and will involve research, development and production.

Candidates should possess a good honours degree in Biochemistry, or in Chemistry with Physiology. Some knowledge of statistics and some research experience are desirable, but not essential.

Applications should be made to the Head of the Immunology Department, The Wellcome Research Laboratories, Beckenham, Kent, from whom additional information can be obtained.

UNIVERSITY OF LEEDS

INSTITUTE OF EDUCATION

Applications are invited from suitably qualified men and women for the post of Lecturer in Education at a salary on the scale £1,050 by £50 to £1,400 by £75 to £1,850 (efficiency bar at £1,550) a year according to experience and qualifications. Candidates should be well qualified and have had experience in the teaching of Science. Preference will be given to those with qualifications in Physics or Chemistry. The principal duties of the Lecturer appointed will be to endeavour to develop the teaching of Science in the area of the Institute as a whole.

Applications (three copies), stating date of birth, qualifications and experience, together with the names of three referees, should reach the Registrar, the University, Leeds, 2 (from whom further particulars may be obtained), not later than April 6, 1961.

UNIVERSITY OF SHEFFIELD

Applications are invited for a post of Lecturer in Metallurgy to begin duties as soon as possible. Ph.D., or equivalent experience in metallurgy is desirable, or in pure science if interests and experience are related to metals. Initial salary according to qualifications and experience on the scale £1,050 by £50 to £1,400 by £75 to £1,850, with F.S.S.U. provision and family allowance. A grant towards removal expenses will be made.

Further particulars may be obtained from the Registrar, to whom applications (four copies), should be sent by April 30, 1961.

BOURNEMOUTH EDUCATION COMMITTEE

BOURNEMOUTH MUNICIPAL COLLEGE OF TECHNOLOGY AND COMMERCE
DEPARTMENT OF SCIENCE

Lecturer in Chemistry required as soon as possible. Applicants should possess good academic qualifications and should be capable of teaching Organic Chemistry to B.Sc. (General) and O.R.I.C. levels. Salary in accordance with the Burnham Technical Scale, viz., £1,370 to £1,550.

CITY GENERAL HOSPITAL

SHEFFIELD, 5

Applications are invited immediately for the post of Senior Technician (Grade I) or Scientific Officer for Microbiological Assay Unit (Vitamin B12 and folic acid). Salary on scale according to grading, i.e., Senior Technician I, £710 to £780; Scientific Officer, £730 to £925 (candidates possessing first- or second-class honours degree or Associate or Graduate Membership of the Royal Institute of Chemistry), or £650 to £925 (candidates possessing other appropriate science degrees). Whitley Council conditions of service.

Apply, giving full details of age, experience, etc., and the names of two referees, to the Group Secretary, Sheffield No. 1 Hospital Management Committee "Lyndhurst," Nether Edge Hospital, Sheffield, 11.

UNIVERSITY COLLEGE OF NORTH WALES

BANGOR

Applications are invited from entomologists for the post of Assistant Lecturer in the Department of Agricultural and Forest Zoology. A special interest in either Ecology or Insect behaviour would be desirable, but not essential. The salary scale is £800 by £50 to £950 per annum and in addition there are F.S.S.U. benefits and family allowances. The appointment will date from October 1, 1961.

Two copies of the application should reach the Registrar, from whom further particulars may be obtained, not later than April 1, 1961.

PHYSICAL CHEMISTS

A research programme of great scope and interest covers high polymers, inorganic and organic pigments, etc., in surface coatings over a variety of substrates. Physical chemists are required for basic work in this field. Previous research experience although desirable is not essential. Salaries will be commensurate with age and experience, with F.S.S.U. superannuation.

Applications, giving full details of qualifications and experience, and the names of two referees, should be made, in writing, to the Director, the Research Association of British Paint, Colour and Varnish Manufacturers, Paint Research Station, Waldegrave Road, Teddington, Middlesex.

UNIVERSITY OF GLASGOW

LECTURESHIP OR ASSISTANTSHIP IN PHYSIOLOGY

Applications are invited for a Lectureship or an Assistantship in Physiology. Salary scale: With a medical qualification, £1,050 to £1,900 per annum for Lecturers, and £1,050 to £1,250 per annum for Assistants; without a medical qualification, £1,050 to £1,850 per annum for Lecturers, and £800 to £950 per annum for Assistants. Initial salary according to experience and qualifications. F.S.S.U. and family allowance benefits.

Applications (eight copies for the Lectureship, three copies for the Assistantship) should be lodged, not later than April 29, 1961, with the undersigned, from whom further particulars may be obtained.

ROBT. T. HUTCHESON,
Secretary of University Court.

UNIVERSITY OF LONDON: APPLICATIONS are invited for Imperial Chemical Industries Research Fellowships in Biochemistry, Chemistry, Chemotherapy, Engineering, Metallurgy, Pharmacology or Physics. The Fellowships will normally be tenable from October 1, 1961, for three years. Candidates should preferably have a Ph.D. degree or equivalent research experience. Stipends will be within the range of £900 to £1,100 per annum, with annual increments of £50 up to £1,100, the starting point within the range being dependent upon experience and qualifications. Family allowance and F.S.S.U.—Detailed regulations and application forms may be obtained from the Academic Registrar, University of London, Senate House, W.C.1. Applications must be received not later than April 15, 1961.

RESEARCH CHEMIST WANTED BY FIRM producing alloys and compounds of the "rarer" metals. The work will include investigation of treatment on both laboratory and pilot plant scale. An interest in new analytical methods would be an advantage (spectrographic, spectrophotometric and chromatographic methods are in routine use in the laboratory). Applicants should have at least a second-class honours degree or equivalent, but initiative and originality are more important than previous research experience. Starting salary approximately £1,000 per annum. Three weeks' annual holiday. A pension scheme is in operation.—Apply to London and Scandinavian Metallurgical Co. Ltd., Fullerton Road, Rotherham, Yorkshire.

NEW ZEALAND
AGRICULTURE DEPARTMENT

Applications are invited for the undermentioned vacancy. Vacancy No. 227. Scientific Officer, Levin, Horticultural Research Station, Agriculture Department, New Zealand. Salary up to £1,210 according to qualifications and experience. Further promotion would be on scientific merit and an outstanding officer may reach £2,300. Duties: The appointee will be a member of the Diagnostic and Research Group at Levin. Research and general experimental work in the field of problems associated with ornamentals and flowers and preparation of material for publication. Some plant identification and advice in connection with the introduction of plants into New Zealand is also involved. Qualifications: Applicants must hold a recognized degree in horticulture, science or agriculture, with a good knowledge of plant families. Passages: Steamer fares of up to £165 each for the appointee and his wife, and pro rata for dependent children will be paid. Incidental expenses: Up to £35 for a single person and £100 for a married man can be claimed to cover the cost of taking personal effects to New Zealand.

Application forms and further details are available from the High Commissioner for New Zealand, 415 Strand, London, W.C.2, with whom applications will close on April 16, 1961. Please quote reference B13/2/2 when inquiring.

RESEARCH FELLOWSHIP IN PHARMACOLOGY

On the retirement of Professor J. H. Burn from the Chair of Pharmacology at Oxford in 1959 his colleagues contributed to a Trust Fund to commemorate his work. Applications are now invited for the post of Burn Research Fellow in Pharmacology at Oxford. Applicants should be less than 30 years old and should be graduates with two to three years research experience. The Fellowship will be tenable for one year from October 1, 1961, and would be renewable for a further two years at the discretion of the Trustees. The remuneration will be £800 to £1,000 per annum.

Applications to the Secretary to the Trustees, Department of Pharmacology, University of Oxford, before May 15, 1961.

BUILDING RESEARCH STATION, D.S.I.R., Garston, near Watford, Herts., requires Assistant Experimental Officer to join team working in field of building design, to assess extent to which physical environment provided in buildings satisfies occupants and thus provide basis for recommendations to designers. Duties include assisting in social surveys and field experiments and analysing results obtained. Qualifications, pass degree in psychology or social science or in natural science, or equivalent. Salary £625 (age 22) to £776 (age 26) to £957, with promotion prospects to £1,336.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting Reference G67/1A. Closing date April 4, 1961.

ASSISTANT BACTERIOLOGIST (SCIENCE Graduate) required for University Department of Bacteriology at the Western Infirmary, Glasgow. Whitley Council salary scale (probationary scale (first two years), ordinary degree, £650 to £925, first- and second-class honours degree £730 to £925, basic scale £925 to £1,150), and conditions of service.—Full particulars from Medical Superintendent, Western Infirmary, Glasgow, to whom applications should be made in writing not later than 14 days after the appearance of this advertisement.

ROYAL FREE HOSPITAL SCHOOL OF Medicine (University of London), Hunter Street, W.C.1. Applications are invited for the post of Lecturer in Biology, with experience in Radiobiology, from October 1, 1961, or as soon after as possible. Salary scale £1,050 to £1,550, then subject to review, £1,850, plus £60 London allowance, with superannuation and family allowances. Further particulars from the Secretary.—Applications to be submitted not later than April 10.

TECHNICIAN REQUIRED FOR RESEARCH Department of Immunology. Biochemical experience desirable. Whitley scales, superannuation under F.S.S.U., commencing date May 1, 1961.—Applications, giving full details of experience, etc., should be addressed to the Secretary, Wright-Fleming Institute, St. Mary's Hospital Medical School, Paddington, W.2, to reach him not later than April 10, 1961.

SENIOR TECHNICIAN I REQUIRED FOR work in Bacteriological Division at Connaught Hospital, Walthamstow, E.17. Whitley Council Scales and Conditions.—Forms of application may be obtained from Secretary, Forest Group H.M.C., Langthorne Road, E.11.

UNIVERSITY OF LONDON
KING'S COLLEGE

The College will require, on October 1, 1961, an Assistant Lecturer in Mathematics. Applicants should have a good Honours degree in Mathematics. An interest in Numerical Analysis will be welcome but not necessary.

Salary scale: £800 by £50 per annum to £950. A London allowance of £60, family allowances, and F.S.S.U. benefits will also be payable.

Full conditions of appointment and application forms may be obtained from the Registrar, King's College, London, Strand, W.C.2, completed forms must reach him by April 17.

UNIVERSITY OF LIVERPOOL

Applications are invited for the post of Assistant Lecturer or Lecturer in the Department of Oceanography. Candidates should have an honours degree in Physical Oceanography or Physics, and should be prepared to spend several weeks each year at sea. The initial salary will be within the range £800 to £1,350 per annum, according to age, qualifications and experience.

Applications, stating age, academic qualifications and experience, together with the names of three referees, should be received not later than April 4, 1961, by the Registrar, from whom further particulars of the conditions of appointment may be obtained. Quoting reference CV/N.

PAINT RESEARCH STATION
ORGANO-METALLIC COMPOUNDS

Chemists are invited to apply for a post in a special project to study the role of organometallic compounds in paint. The work, mostly fundamental in character, will include both organic and physico-chemical studies. Applicants should have a good honours degree; a Ph.D. or equivalent research experience is desirable. Salaries will be commensurate with age and experience, with F.S.S.U. superannuation.

Applications, giving full details of qualifications and experience, and the names of two references, should be made in writing to the Director, The Research Association of British Paint, Colour and Varnish Manufacturers, Paint Research Station, Waldegrave Road, Teddington, Middlesex.

ONTARIO VETERINARY COLLEGE
GUELPH, ONTARIO, CANADA

Applications are invited for an appointment as an Assistant or Associate Professor in Pharmacology. Applicants should have a Ph.D. and teaching experience. The candidate will lecture to undergraduate and postgraduate students in pharmacology and be expected to undertake research in some aspect of the field.

A curriculum vitae and references should be addressed to Dr. H. G. Downie, Professor and Head, Department of Physiological Sciences.

OLDCHURCH HOSPITAL ROMFORD, ESSEX
(709 Beds)
RADIOTHERAPY DEPARTMENT

Senior Technician or Technician required for the above Department. Duties include Physics Workshop, Isotope Laboratory, Radium and Mould Room work. Instrument or Physics Workshop experience essential. Salary £570 to £710 per annum; senior grade, £710 to £905 per annum would be applicable to suitably qualified person.

Applications, quoting Ref. 17/39, giving full details, including age and experience, together with names of two referees and/or copy of testimonials to the Group Secretary, Romford H.M.C., Oldchurch Road, Romford.

UNIVERSITY OF ALBERTA
DEPARTMENT OF CHEMISTRY
TEACHING ASSISTANTSHIPS

$2,200 to $2,700 for eight months are open to qualified students proceeding to advanced degrees. Nine hours per week of laboratory instruction required. Active research programmes in analytical, inorganic, organic, physical and theoretical chemistry. Travel allowance.

Apply to: Professor Harry E. Gunning, Head, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada.

UNIVERSITY OF SYDNEY
MCCAUGHEY CHAIR OF GEOGRAPHY

Applications are invited for the McCaughey Chair of Geography. This Chair will become vacant on the retirement of the present occupant, Professor J. Macdonald Holmes. Salary will be at the rate of £A.4,250 per annum, plus cost of living adjustments (at present £A.36 per annum). There is retirement provision under either the Sydney University Professorial Superannuation Scheme or the New South Wales State Superannuation Scheme. Under the Staff Members' Housing Scheme, in cases approved by the University and its Bankers, married men may be assisted by loans to purchase a house. The Senate reserves the right to fill the Chair by invitation.

A statement of conditions of appointment and information for candidates may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close in Australia and London on May 31, 1961.

BRITISH COUNCIL
UNIVERSITY OF CHILE

Applications are invited for the post of Research Consultant in the Centre of Chemistry at the University of Chile, Santiago. Duties, to conduct and advise on research, to advise on the organization of the Centre, and to conduct courses for the research staff. Candidates must have sound British academic qualifications, and should have specialized in physical or inorganic chemistry. Salary on scale £1,980 by £75 to £2,430. Overseas allowance (maximum): Single, £595; married, £1,125. Children's and home education allowances. Free furnished accommodation. Installation grant. Employer's portion U.K. superannuation paid. Medical scheme. Contract with University and British Council for two years, renewable. Fares paid, and for family (including mid-tour passages for children in U.K.). Secondment from home employment may be arranged.

Write, quoting N.4.N(61) and enclosing stamped, addressed, foolscap envelope, to Director, Recruitment Department, The British Council, 65 Davies Street, London, W.1, for further particulars and application form to be returned completed within two weeks of receipt.

UNIVERSITY OF EXETER

Applications are invited for the post of Lecturer or Assistant Lecturer in Zoology. Salary scales: Lecturer, £1,050 to £1,850 per annum (efficiency bar at £1,475); Assistant Lecturer, £800 to £950 per annum.

Further particulars may be obtained from the Secretary of the University, to whom applications (eight copies—overseas applicants one copy), giving the names of three referees, should be sent by April 10, 1961.

PERSONAL ASSISTANT/SECRETARY REquired for Head of Physiology Department, National Institute for Research in Dairying. Good secretarial qualifications and some relevant experience, or knowledge of biological science essential. A university degree (preferably in biological science) or equivalent desirable. Commencing salary according to age in scale £469 (age 21) to £568 (age 25 or over on entry) to £796 or for degree in biological science or equivalent, £578 (age 21) to £776 (age 26 or over on entry) to £983, with superannuation in each case.—Applications, naming two referees, to Secretary, N.I.R.D., Shinfield, Reading. Quote reference 61/10.

THE AGRICULTURAL RESEARCH Council requires a Scientific Officer or Senior Scientific Officer for research into aspects of cellular structure and function at their Institute of Animal Physiology. Good second-class honours degree essential; postgraduate experience, training in cytochemical and biochemical techniques and experience in tracer methods desirable. Salary within scales £717 to £1,222 or £1,302 to £1,654 according to experience. F.S.S.U.—Applications, with names of three referees, to the Secretary of the Institute, Babraham, Cambridge, within four weeks.

ENGLISH CLAYS LOVERING POCHIN and Co. Ltd., have a vacancy in their Research Department for a Science Graduate interested in the field of Physical Chemistry.—Applications, giving full career and personal particulars, should be addressed to the Personnel Officer, 14 High Cross Street, St. Austell, Cornwall.

STUDENT TECHNICIAN REQUIRED IN the Department of Pathology, Connaught Hospital, Walthamstow, E.17. Facilities for training and study for the examination of the I.M.L.T. Salary in accordance with Whitley Scales.—Forms of application may be obtained from Secretary, Forest Group H.M.C., Langthorne Road, E.11.

BISRA

TWO-YEAR GRADUATE APPRENTICESHIPS IN OPERATIONAL RESEARCH

A number of these apprenticeships will be offered to graduates with good degrees in engineering, science, mathematics, statistics or economics. In the first year which starts in September, 1961, the trainees will join teams operating throughout the steel industry from the BISRA O.R. Department in Battersea, London. A full-time course in specialized techniques has been arranged with the London School of Economics for the second year, terminating in an examination for the Diploma in Operational Research. All fees will be paid by BISRA and trainees will additionally receive a fixed salary in the range £700 (at age 21) to £800 (at the ceiling age of 25). Prospects for diploma holders are excellent both in the steel industry and outside. Interested graduates under 26, including those expecting good honours degrees in 1961, should apply for particulars and application form to:

The Personnel Officer, The British Iron and Steel Research Association, 11 Park Lane, London, W.1.

NATIONAL COLLEGE FOR HEATING, VENTILATING, REFRIGERATION AND FAN ENGINEERING

AT THE BOROUGH POLYTECHNIC, BOROUGH ROAD, LONDON, S.E.1

Director: James E. Garside, M.Sc.Tech., Ph.D., F.R.I.C., F.I.M., F.Inst.F.

Head of College: David R. Scott, M.Sc., Ph.D., M.Inst.R., A.M.I.H.V.E., A.Inst.P., A.M.I.Mech.E., A.M.E.M.E.

BRITISH REFRIGERATION ASSOCIATION RESEARCH FELLOWSHIP

The Governors invite applications from graduates or from those graduating this year in Engineering or Physics for the above Fellowship, tenable at the National College. The successful applicant will be required to undertake research on Heat Transfer in Refrigeration Evaporators. The value of the Fellowship is at present £800 per annum, as this is a Fellowship the income is not taxable; the Fellowship is awarded for a minimum period of two years. Should he desire, the Fellow will be further permitted to undertake six hours lecturing per week, which would augment his income by approximately £150 per annum. The value of the Award is under review and may be subject to an increase after one year. Where University regulations permit the Fellow will be encouraged to present his work for a higher degree. The Fellowship provides a suitable opening for an ambitious young man wishing to enter the small, but well-paid, field of Refrigeration Engineering in which many excellent opportunities exist.

Further information is obtainable from the undersigned, to whom application should be made as soon as possible.

FREDK. J. PACKER,
Clerk to the Governors.

UNIVERSITY OF BIRMINGHAM

ASSISTANT SECRETARY, APPOINTMENTS BOARD

Applications are invited for the post of Assistant Secretary (Science) to the Appointments Board. The appointment, to commence on a date to be agreed, probably in the late summer, will be made within the salary range £1,250 to £1,850 with F.S.S.U. and family allowance benefits. Applicants should be graduates and preference may be given to those who have had some industrial or other relevant experience.

Applications, giving the names of three referees, should be sent by April 12, 1961, to the undersigned from whom further particulars may be obtained.

P. C. HORDERN,
Secretary to the Appointments Board.

The University,
Birmingham, 15.

COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES

(C.I.O.M.S.)

invites applications for the position of

EXECUTIVE SECRETARY

The Executive Secretary, who is responsible for the administration of the Council, must be highly qualified in medical organization. Applicants should have a university degree in medicine. Administrative experience and ability to collaborate with other international organizations are required. Fluent knowledge of English and French is required. Further languages are an additional qualification. The Secretariat is in Paris, where the successful candidate is expected to take up residence. The starting salary will be according to experience and qualification and will be not less than U.S.$7,000 per annum.

Applications should reach Professor J. Maisin, Institut du Cancer, 57 voer des Capucins, Louvain, Belgium, before May 1, 1961. Two references for confidential consultation by the Council should be given. Further particulars about the position can be supplied on request.

BOURNEMOUTH EDUCATION COMMITTEE

BOURNEMOUTH MUNICIPAL COLLEGE OF TECHNOLOGY AND COMMERCE

DEPARTMENT OF SCIENCE

Required for September 1, 1961, Assistant Grade "B" to teach Mathematics, principally at G.C.E. "O" and G.C.E. "A" levels, although some more advanced work can be made available. Previous teaching experience is desirable. Salary in accordance with the Burnham Technical Scale, viz.: £700 by £27 10s. to £1,150 per annum, plus additions for qualifications, training and industrial experience.

Further particulars and form of application may be obtained from the Chief Education Officer, Town Hall, Bournemouth.

UNIVERSITY OF WESTERN ONTARIO

LONDON, CANADA

Applications are invited for two appointments to the staff of the Department of Mathematics. Full qualifications include Ph.D. degree in mathematics. Algebraist and analyst preferred. Initial appointments with the rank of Assistant Professor, effective July 1, 1961, teaching duties to commence in September. Life and hospitalization insurance effective at beginning of teaching duties. Pension plan entered after two-year probationary period. Also available four Teaching Fellowships for graduate study in mathematics.

Address applications with two references to Department of Pure and Applied Mathematics, University of Western Ontario, London, Canada.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

A post is available for a physiologist or zoologist, with interests and experience in the field of mammalian reproduction, in a small unit investigating the biochemical and physiological properties of cervical secretions, with particular reference to fertility. The work envisaged will involve a study, in co-operation with two biochemical colleagues, of the metabolism, motility and fertility of spermatozoa in cervical mucus and in fractions which can be separated from it. Good research facilities are available and the post offers an attractive opportunity for a scientist who wishes to work in a field bearing on this highly significant problem. The candidate will be expected to initiate and carry out work on the physiological side of the investigation.

Applicants should have a good degree in zoology or physiology, preferably with Ph.D. Appointment would be for three years in the first instance, salary in accordance with experience and qualifications. Applications to the Secretary, National Institute for Research in Dairying, Shinfield, Reading, Berks. Quote ref. 61/2.

SCIENTIFIC PUBLISHERS ENGAGED ON cover-to-cover translation of Russian chemical literature require an Assistant Editor with sound knowledge of scientific Russian and a good degree in chemistry. Salary up to £2,000 a year according to qualifications. Part-time translators from Russian with a degree in chemistry also required.—Apply to Infosearch Ltd., 207 Brondesbury Park, London, N.W.2.

GLACIER METAL CO., LTD., Kirkstyle, Kilmarnock, Scotland,

invite applications for the position of

PHYSICAL CHEMIST

A Physical Chemist is required for the Metallurgy Department of the Research and Development Organization.

He will investigate the physical and chemical phenomena which determine the frictional behaviour and wear resistance characteristics of new non-metallic bearing materials.

The successful applicant will be responsible for deciding his own lines of work within his own field, and for the design and analysis of his experiments.

He will be a member of a vigorous and expanding research organization which has achieved considerable success in the development of bearing materials.

Applicants must have a Degree in Inorganic or, preferably Physical Chemistry, and some experience of Surface Chemistry is essential. The preferred age range is 24 to 30 and both men and women are eligible for consideration.

The salary range is £938 to £1,384 and a starting salary up to £1,175 is envisaged.

Write for application form to Personnel Department, quoting reference 3/RDO/3/22.

JOSEPH CROSFIELD & SONS, LIMITED

WARRINGTON

Requires a

RESEARCH CHEMIST

Research Chemist required to work on colloidal aspects of silicates and silica and the influence of some forms of organic polymerizations on these colloidal states.

Candidates should be fully qualified and possess good experimental ability. Experience in industrial research would be an advantage, though is not essential.

Applications, giving full details of qualifications and experience should be made, in writing, to the Personnel Manager, Joseph Crosfield and Sons Limited, Bank Quay Works, Warrington.

PHARMACOLOGIST

required to work in London for the first two years in an academic department and thereafter in a newly created Research Laboratory in London.

Non-contributory Pension and Life Assurance Scheme and excellent salary; scope for promotion.

Write, giving full details of age, qualifications, experience and salary required, to The Managing Director, Biorex Laboratories Ltd., 47/51 Exmouth Market, London, E.C.1.

UNIVERSITY OF GLASGOW

Applications are invited for the post of Tutor in the Department of Extra-Mural Education; candidates should have qualifications in Natural or Physical Science; experience in extra-mural work, while not essential, will be an advantage. Salary scale £1,050 to £1,850; initial salary according to experience and qualifications; F.S.S.U. and family allowance benefits.

Particulars may be obtained from the Secretary of the University Court, the University, Glasgow, W.2, to whom applications should be returned by April 10, 1961.

UNIVERSITY OF TASMANIA
RESEARCH FELLOWSHIP IN PHYSICS

Applications are invited from graduates with research experience for a Research Fellowship in Physics. Commencing salary will be within the range £A.1,400 to £A.1,600. The Fellow will participate in a new programme of research in radio physics, including low frequency radio-astronomy, and the radio emissions of the earth's outer atmosphere. Large radio telescopes for use in the programme are under construction.

Further information is available from D. A. Kearney, the Acting Registrar, Box 252C, G.P.O., Hobart, Tasmania.

UNIVERSITY OF TASMANIA
LECTURER OR SENIOR LECTURER IN MATHEMATICS

Applications are invited from pure or applied mathematicians for appointment to a Lectureship or Senior Lectureship in Mathematics. Salary scales are: Lecturers, £A.1,650 by £A.70 to £A.2,350 and Senior Lecturers, £A.2,450 by £A.60 to £A.2,870. Appointment will be offered within the grades according to qualifications and experience.

Further particulars and information as to the method of application are available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on May 15, 1961.

UNIVERSITY OF GLASGOW
UNIVERSITY STUDENTSHIPS AND FELLOWSHIPS

Applications are invited for University Studentships and Fellowships for experimental or theoretical research in Nuclear and Elementary Particle Physics. Salary scale: Studentships, £350 to £600 per annum, according to qualifications, with a tenure of three years. Fellowships, £700 to £1,000 per annum, according to qualifications. Tenure three years on appointment, with possible renewal for further period of two years. These Fellowships will be superannuated under the F.S.S.U.

Applications, stating age, academic qualifications, research experience and names of two referees, should be sent to the Professor of Natural Philosophy, University of Glasgow, before April 29, 1961.

UNIVERSITY OF TASMANIA
CHAIR OF AGRICULTURE

The University invites applications for appointment as First Professor of Agriculture at a salary of £A.4,000 per annum. The Council of the University has created the Chair of Agriculture as a first move in the establishment of a Faculty of Agriculture, and the Professor will be expected to advise the Council on the organization of courses and the staff required.

Further particulars and information as to the method of application are available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on May 31, 1961.

COMMONWEALTH AGRICULTURAL BUREAUX
VACANCY ON THE STAFF OF THE COMMONWEALTH INSTITUTE OF ENTOMOLOGY
56 QUEEN'S GATE, LONDON, S.W.7

Science graduate required, primarily to assist in the production of the *Review of Applied Entomology*. The qualifications sought are a good honours degree with experience, preferably overseas, in economic entomology, and ability to write lucid and concise English précis and to read two other European languages. Starting salary according to experience and qualifications in the scale £759 to £1,704 per annum, with possibility of further promotion. Superannuation scheme.

For further details apply before May 15, 1961, to the Secretary, Commonwealth Agricultural Bureaux, Farnham House, Farnham Royal, near Slough, Bucks, England.

ASLIB REQUIRES TWO RESEARCH Assistants (one senior) for investigations into special, mainly scientific, library and information problems. Both should, preferably, be graduates with some knowledge of statistical methods and the design of experiments. Candidates for the senior post should have had some research experience and be capable of planning and carrying out investigations and presenting the results. Salary ranges £1,000 to £1,500 and £670 to £1,000, plus superannuation.—Apply to Director, Aslib, 3 Belgrave Square, London, S.W.1.

UNITED COLLEGE
WINNIPEG, MANITOBA, CANADA

Mathematics Instructor required to teach undergraduates in liberal arts college. M.A. or M.Sc. required.

For details write Dean E. D. Eagle, United College, Winnipeg 2, Manitoba, Canada.

APPLICATIONS ARE INVITED FOR POSITIONS of Research Chemist and Senior Technician.—Please apply to the Secretary, Middlesex Hospital Medical School, London, W.1, quoting the date of this advertisement.

CHEMISTRY DEPARTMENT, UNIVERSITY of Southampton. Applications are invited for the Union Carbide Postdoctoral Fellowship in Organic Chemistry. Salary £850 to £1,000 per annum tenable for up to three years.—Applications, giving details of qualifications and names of two referees, should be sent to Professor R. C. Cookson, The University, Southampton.

TRADE ANNOUNCEMENTS

BRIGHT'S REMOTE COLD CONTROLLED Microtome (cryostat) custom built for producing frozen sections for rapid diagnostic biopsies.—Full information on request to Bright's Refrigerator Service Ltd., 399 Portobello Road, London, W.10. LADbroke 4153.

MICROSCOPES. GOOD SECONDHAND Microscopes from £10 to £100, various makes and types for medicine, biology, pharmacy, botany. Tested by the specialists Wallace Heaton Ltd., 127 New Bond Street, London, W.1.

LECTURES AND COURSES

UNIVERSITY OF EDINBURGH
PLANT TAXONOMY

A vacation course in the practice of plant taxonomy, including a taxonomic revision, will be given from August 28 to September 8.

For particulars apply to Dr. P. H. Davis, University Department of Botany, Royal Botanic Garden, Edinburgh, 3.

For qualified

SCIENTISTS, ENGINEERS, ARCHITECTS AND SURVEYORS

THE TECHNICAL AND SCIENTIFIC REGISTER

provides a National Employment and Advisory Service. All enquiries are dealt with in confidence by professionally qualified staff.

A leaflet, giving details of the Service, will be sent on request.

Write for information or appointment to

THE TECHNICAL AND SCIENTIFIC REGISTER, Dept. K.10, Almack House, 26 King Street, London, S.W.1.

Telephone: WHI 6200 (Ext. 328)

Issued by the Ministry of Labour

UNIVERSITY OF LONDON

ST. BARTHOLOMEW'S HOSPITAL MEDICAL COLLEGE

Charterhouse Square, London, E.C.1

M.Sc. COURSE IN RADIATION BIOLOGY

A course for this degree will commence in October, 1961. It normally extends over two academic years and will consist of lectures and laboratory work in radiation physics, chemistry and biochemistry, radiobiology, medical and industrial applications of radiation and the principles and practice of the control of radiation hazards. Candidates should have either a B.Sc. honours degree in a science subject or a medical degree.

A small number of full-time Studentships of £400 per annum plus fees will be available from the D.S.I.R. The fees are 30 guineas per term.

Applications should be addressed to the Secretary of the Medical College, from whom further particulars may be obtained.

UNIVERSITY COLLEGE OF WALES

ABERYSTWYTH

POSTGRADUATE DIPLOMA IN "PHYSICS OF THE ATMOSPHERE"

The Departments of Applied Mathematics and Physics expect to offer in session 1961-62 a one-year course leading to a Diploma in "Physics of the Atmosphere." The course will be open to students of postgraduate standing of any recognized University, College or Institute whose undergraduate courses have, in the opinion of the Departments concerned, included a suitable preliminary training. The course will include the following: Upper Atmosphere Physics; Geomagnetism; Dynamical Meteorology; Magnetohydrodynamics; Dynamics of the Ionosphere.

Further particulars may be obtained from the Registrar, University College of Wales, Aberystwyth.

NATIONAL COLLEGE FOR HEATING, VENTILATING, REFRIGERATION AND FAN ENGINEERING

ADVANCED HEAT TRANSFER

Postgraduate Courses of Ten Lectures by E. Woodcock, M.Sc.

(Lecturer in Heat Transfer at the National College)

(i) Drying (and the theory of heat and mass transfer) commences Monday, April 10, 1961.

(ii) Refrigeration (heat and mass transfer) commences Tuesday, April 11, 1961.

Syllabus and application forms from: The Clerk to the Governors, National College H.V.R.F.E., Borough Polytechnic, Borough Road, London, S.E.1.

UNIVERSITY COLLEGE LONDON

BIOCHEMICAL ENGINEERING

A one-year postgraduate course leading to a College Diploma is starting on October 2, 1961, suitable for men with degree in Chemical Engineering, Biochemistry, or other associated subjects. The syllabus deals specially with theoretical and practical aspects of food and pharmaceutical manufacture and is intended for those wishing to take responsible positions in these industries, either in direct management or development.

Inquiries to Professor M. B. Donald, Department of Chemical Engineering, University College London, Gower Street, W.C.1.

GRANTS & SCHOLARSHIPS

UNIVERSITY OF DUBLIN

TRINITY COLLEGE

LEFROY STEIN SCHOLARSHIP

A Lefroy Stein Scholarship for research in any of the Biological or Medical Sciences will shortly be awarded by Trinity College. The scholar will be expected to devote his full time to research in Trinity College in one of the above fields, and will receive a stipend of £400 per annum. Applicants should be graduates of a recognized university, preferably under 26 years of age. The scholarship will be tenable for two years from September 21, 1961.

Applications (three copies), on the prescribed forms, should reach the Registrar, Trinity College, Dublin 2, from whom further particulars and application forms may be obtained, not later than May 1, 1961.

UNIVERSITY OF EDINBURGH

STUDENTSHIPS AND FELLOWSHIPS

Studentships and Junior and Senior Fellowships, open to graduates of any University and tenable in the Faculties of Divinity, Law, Medicine, Arts, Science and Music of the University of Edinburgh, will be available for award in session 1961-62. Up to six awards may be made. The value of a Postgraduate Studentship is £300; if renewed for a second and third year £320 and £340 respectively. The value of a Junior Fellowship is £500; if renewed for a second and third year £550 and £600 respectively. The value of a Senior Fellowship is £750; if renewed for a second and third year £800 and £850 respectively. Applications must be submitted through the Dean of the appropriate Faculty before April 15, 1961.

Further particulars and application forms may be obtained from the Secretary to the University, Old College, South Bridge, Edinburgh, 8.

CHARLES H. STEWART,
Secretary to the University.

MERTON COLLEGE OXFORD

POSTGRADUATE SCHOLARSHIP

The College proposes to elect on July 29, 1961, if a candidate of sufficient merit presents himself, to one SENIOR SCHOLARSHIP open to male graduates of universities or university colleges in the British Isles other than Oxford and Cambridge, without restriction of subject. The scholarship will be tenable for two years from October 1, 1961, at which date candidates must have qualified for a university degree and must be under 26 years of age. The scholar will be required to read for the degree of Doctor of Philosophy or to pursue such other postgraduate course in the University of Oxford as the College may approve, and to reside in Oxford during the academic terms. The annual value of the scholarship will be £500, subject to reduction if other awards are held concurrently.

Intending applicants should write in the first instance to the Senior Fellow, Merton College, Oxford, briefly indicating their present academic status and their proposed course of postgraduate study. Each letter must be accompanied by a statement signed by the head of the applicant's university or college to the effect that the application is made with his approval. Entry forms and further particulars will then be sent to those applicants whose proposed courses of study are approved. The closing date for applications is May 15, 1961.

UNIVERSITY OF LONDON

KING'S COLLEGE

CHEMICAL ENGINEERING

The Department offers Shell Studentships of £375 plus tuition fees for the one-year postgraduate course for the College Diploma in Chemical Engineering.

Advanced Course Studentships offered by D.S.I.R. may also be held in the Department.

Applications are invited from graduates in Chemistry or Engineering. Forms must be obtained from the Registrar, King's College, Strand, London, W.C.2, and must reach him completed, by April 17.

UNIVERSITY OF READING

J. J. THOMSON PHYSICAL LABORATORY

The Department of Scientific and Industrial Research is prepared this year to offer to suitable candidates a limited number of research studentships tenable in the J. J. Thomson Physical Laboratory of the University of Reading. The value of these awards will be £340 per annum. Fees are paid by the D.S.I.R., a small travelling allowance is paid and a student may earn up to £50 per annum as a student demonstrator. The vacancies which exist are for work on various topics in solid state physics and physiological optics. Candidates should have a good honours degree in physics. Other awards are available, including some which are suitable for applicants who have already had experience of research.

Applications should be sent, by May 12, 1961, to Professor Ditchburn, J. J. Thomson Physical Laboratory, Whiteknights Park, Reading.

ANIMAL HEALTH TRUST

RESEARCH TRAINING SCHOLARSHIPS 1961

A few Research Training Scholarships are offered by the Animal Health Trust to recent Graduates in Veterinary Medicine or Natural Science. These Scholarships to the value of £500 per annum will be exempt from income tax and will carry a grant not exceeding £60 per annum towards the payment of essential fees. Applicants must be desirous of entering upon a research career connected with Veterinary Medicine.

Forms of application can be obtained from The Scientific Director, The Animal Health Trust, 14 Ashley Place, London, S.W.1. The closing date for the receipt of applications is May 12, 1961.

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Further particulars, and application forms which must be returned before May 15, 1961, obtainable from Registrar, Imperial College, London, S.W.7.

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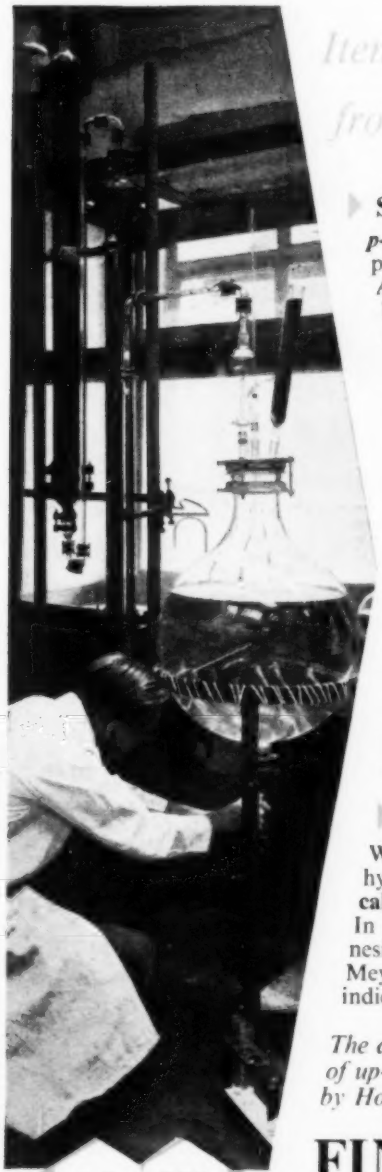

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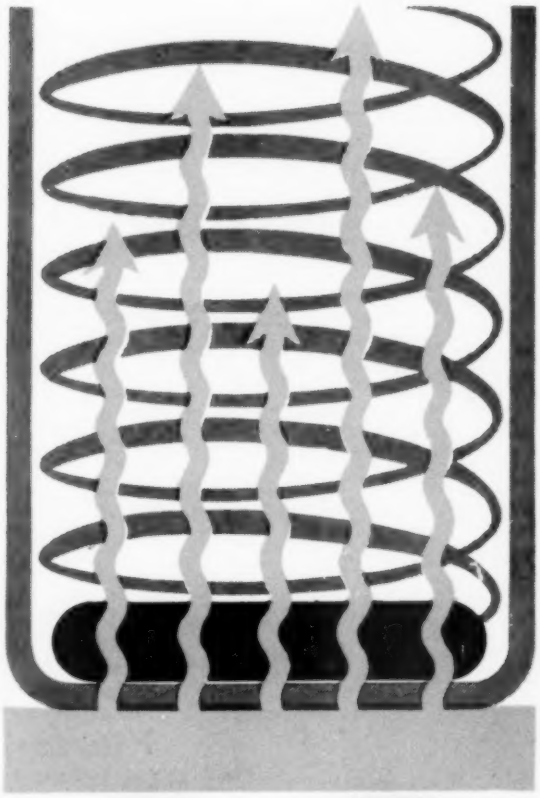

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